A SINGLE UNIT ANALYSIS OF NEURAL PLASTICITY IN ADULT CATS: EFFECTS OF MONOCULAR PARALYSIS ON THE LATERAL GENICULATE NUCLEUS

by

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APPROVAL PAGE

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Loss of binocularity has been reported selectively in simple cortical cells following chronic monocular paralysis in adult cats. The nature of any analogous changes which may occur in the dorsal lateral geniculate nucleus (LGNd) may be predicted by the parallel processing model of geniculostriate connections. This model predicts that if simple cortical cells are selectively affected by chronic monocular paralysis, then the X-cell population of the LGNd should be affected selectively if any effect is seen. This experiment, therefore, examined the effects of chronic monocular paralysis in adult cats on the X- and Y-cell populations of the LGNd.

Under sodium pentobarbital anesthesia one eye in each of 10 adult cats was immobilized by transection of cranial nerves III, IV and VI. At the same time the skull was prepared for semi-chronic microelectrode recording. After paralysis of varying duration with otherwise normal visual experience, single unit recordings were made in the LGNd. The paralyzed eye was focused on a tangent screen. Receptive fields of single units were mapped and classified as X or Y on the basis of standard criteria.

In the first phase of the experiment, recordings were made at either 1-3 days following surgery (acute monocular

paralysis) or at periods of 16 days or more (chronic monocular paralysis). These intervals were chosen to place the observations clearly on either side of the 7-8 day period reported previously to be critical for the changes in simple cortical cells. Different subjects were used in each condition to eliminate the effects of sequential recording. In the acute condition the proportions of X- and Y-cells recorded were roughly equal. These results are in good agreement with other reports in acutely paralyzed animals. When recordings were made at 16 days or more of monocular paralysis, however, these percentages were drastically altered. Only about 6% of the units encountered were X-cells.

In a second phase of the experiment the time course for this loss of X-cells in the LGNd of adult cats following chronic monocular paralysis was studied. After day 3, a drop in the percentage of X-cells was noted. From day 4 to day 15 only about 30% of the cells recorded were X-cells. After day 15 another drop in the percentage of X-cells was seen, leaving only the 6% recorded in the chronic condition.

These results, then, are interpreted as indicating that the effects of monocular paralysis on visual experience produced a decrease in the number of functional X-cells in the adult cat's LGNd. Furthermore, this loss appears to occur in two stages, one about 4 days after the onset of the paralysis and the other about day 16. These two points

of loss, one occurring on either side of the cortical effect, may suggest a dual mechanism for the X-cell loss in the LGNd. The first portion of the loss may be initiated in the LGNd and produce the loss in binocularity of simple cells. The later portion, in turn, may be initiated in cortex and transmitted secondarily to LGNd (by corticalfugal fibers).

The attrition of the X-cell population in the LGNd following chronic monocular paralysis provides a new demonstration of neural plasticity in the adult visual system. In addition, these results contribute to the resolution of a number of theoretical issues, particularly the validity of the X/Y distinction and the parallel processing model of connectivity within the geniculostriate system.

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CHAPTER I

INTRODUCTION

The changes which occur in the nervous system as a function of experience have been of sustained interest to physiological psychologists. Such changes reflect nervous system plasticity and are often studied under such rubrics as "learning" or "development."

In recent years the neural plasticity displayed by kittens reared under conditions of abnormal interocular interaction has gained the interest of many neuroscientists A variety of experimental manipulations has been used to disrupt normal visual experience; many have resulted in profound and possibly permanent changes in nervous system organization. The effects of experimentally induced visual insults have been observed in a variety of visual structures including visual cortex (Wiesel & Hubel, 1963a; Wiesel & Hubel, 1965), dorsal lateral geniculate nucleus (LGNd) (Wiesel & Hubel, 1963b; Sherman, Hoffmann, & Stone, 1972), and superior colliculus (Wickelgren & Sterling, 1969a, 1969b; Sterling & Wickelgren, 1970). Before reviewing the experimental manipulations and their effects, however, the properties of neurons in the visual system which have been found to be subject to modification will be briefly summarized.

Selected Properties of Units in Normal (Adult) Visual System

Two properties, common to all cortical units, have been shown to be subject to environmental manipulation. These are orientation selectivity and binocularity. Hubel and Wiesel (1959, 1962, 1965b) reported that all cells in cat visual cortex respond maximally to elongated targets. For any particular cell, however, the appropriate stimulus is effective only when it is oriented in a particular direction. In the adult cat, changing the orientation of the appropriate stimulus by 30° or less from the optimal orientation is sufficient to make that stimulus totally ineffective in driving the cell. Although any given cell responds to only a limited range of orientations, all orientations are represented in cells in normal cat cortex.

Hubel and Wiesel (1962) have also reported that about 80% or more of the cells in normal cat cortex are binocular (i.e., can be driven by stimulation of either eye). A seven step histogram is frequently employed to describe the relative effectiveness of the two eyes in driving each cortical cell. Classes 1 and 7 represent cells which can only be driven monocularly by the contralateral or ipsilateral eyes respectively. For cells in classes 2 and 3, the contralateral eye is dominant and for cells in classes 5 and 6, the ipsilateral eye is dominant.

Cells in class 4 can be driven with equal effectiveness by both eyes.

Aside from the properties of orientation selectivity and binocularity which are common to all cells in the cat's visual cortex and which are relevant to a discussion of plasticity, units may be divided into two types on the basis of the way they respond to the location of the appropriate stimulus. For some cells, termed "simple," the exact position of the stimulus is critical. These cells have small receptive fields and respond maximally to a stimulus of appropriate contrast and orientation which completely fills the elongated center of the receptive field. Hubel and Wiesel (1962) define this class of cortical cells as those which may be mapped with small spot stimulation and their responses to stimuli completely specified by this mapping. Other cortical cells, however, have much more complex receptive field properties. They have much larger receptive fields than simple cells, but do not respond maximally to targets which fill the entire center of the receptive field. These cells, termed "complex," respond most briskly to an appropriate, oriented, target moving in a particular direction which is orthogonal to the elongated axis of the stimulus. They are inhibited by stimuli moving in the opposite direction, a property referred to as "directional selectivity." Hubel and Wiesel (1962) termed cells whose properties may not be

completely specified by mapping with small spot stimulation "complex" cells.

In addition to these properties of cortical cells, there is a set of properties of lateral geniculate neurons which is relevant to a discussion of visual plasticity. Lateral geniculate cells can be classified into two groups based on the way these cells sum the influences of light in the center and surround regions of their receptive fields (Cleland, Dubin, & Levick, 1971). One group (X-cells) sums these influences linearly, while the other group (Y-cells) sums nonlinearly (Enroth-Cugell & Robson, 1966). Later experiments showed two subdivisions of retinal ganglion and lateral geniculate cells based on their responses to many types of stimuli (Cleland, Dubin, & Levick, 1971; Cleland, Levick, & Sanderson, 1973; Fukada, 1971; Fukada & Saito, 1971). These subdivisions were found to be functionally analogous to those used in developing the original X/Y distinction. Conduction velocity and cell body size also appear to distinguish these two classes (Stone & Hoffmann, 1971; Hoffmann, Stone, & Sherman, 1972). Y-cells have shorter conduction times to the lateral geniculate in response to electrical stimulation of the optic chiasm. Presumably, therefore, they have larger axons and cell bodies. The X/Y distinction, then, may well rest on these physiological and anatomical characteristics.

Plastic Effects in Kitten Visual System

There are basically three types of manipulations in which plasticity in the kitten visual system has been demonstrated. These are visual deprivation, disruption of normal binocular vision without deprivation, and restriction of the visual environment. Examples of these types of manipulations and the effects they produce on the nervous system are presented below. They are intended as exemplary of the field, however, not as a comprehensive literature review.

Since the effects of visual deprivation by monocular eyelid suture have been the most thoroughly studied, these will be discussed here in greater detail. In their initial investigation of the effects of monocular deprivation, Wiesel and Hubel (1963a) found that after three months of monocular eyelid suture the vast majority of cells in the visual cortex were monocular and could be driven exclusively by the nondeprived eye. The few cells which could be driven by the deprived eye were abnormal in that they lacked orientation specificity. The morphology of the cortex of the monocularly deprived kittens, however, appeared normal.

When the lateral geniculate nucleus was examined in this original investigation Wiesel and Hubel (1963b) found morphological alterations. They observed an atrophy of cells in the layers of the lateral geniculate nucleus

which received input from the deprived eye. Furthermore, it was found that this atrophy was proportional to the amount of total light deprivation. Other investigators have reported both a loss of large cells and a reduction in the mean cell size in the deprived laminae of the geniculate (Guillery & Stelzner, 1970; Guillery, 1972, 1973; Chow & Stewart, 1972).

In Wiesel and Hubel's (1963b) original physiological investigation of the lateral geniculate of monocularly deprived kittens, however, they found no apparent functional changes to parallel those in cortex. Only much later, when the lateral geniculate was examined with respect to receptive field properties which were unknown to Wiesel and Hubel at the time of their original investigation, were physiological changes found. Using the Hubel-Wiesel monocular lid suture preparation, Sherman, Hoffmann, and Stone (1972) found that the number of Y-cells was markedly reduced in laminae receiving input from the deprived eye. Since, based on the conduction velocity data, Y-cells are presumably the largest cells in the lateral geniculate nucleus, these findings provide a functional significance for the morphological changes described. This reduction in the number of large cells in the LGNd following monocular deprivation can now be explained by the selective loss of Y-cells in deprived laminae.

In terms of the subject's visual experience, disruption of binocular vision without visual deprivation

is a less drastic procedure than deprivation by eyelid suture. Both procedures, however, produce many similar effects. In one experiment Hubel and Wiesel (1965a) disrupted binocular vision by two different methods. In some kittens the medial rectus muscle was severed, producing an extreme divergent squint. Other subjects were raised from the time of normal eye opening with an opaque occluder covering alternate eyes on alternate days. In both of these manipulations each eye received equal patterned input, but there was no chance for normal binocular vision. Both of these manipulations produced similar results at the cortical level. The vast majority of cells in the striate cortex could only be driven monocularly, with each eye being roughly equal in the number of cells it drove. The physiology of the lateral geniculate was not examined after either of these manipulations. The morphology of both the cortex and lateral geniculate, however, appeared normal.

Similarly, experimenters who have restricted the visual environment of kittens have examined neither the physiology nor the morphology of the lateral geniculate. The effects of these manipulations at the cortical level, however, has been studied by several investigators. Blakemore and Cooper (1970) reared kittens with limited visual experience, exposing them to only lines of one

orientation. Such experience biased the population of cortical neurons. Only cells with receptive field orientations close to that experienced could be recorded. A later experiment found that, after dark-rearing, a very brief exposure (as low as 1 hr.) to lines of a single orientation was effective in producing this bias in the cortical neuron population (Blakemore & Mitchell, 1973). Although later studies have failed to replicate these results (Stryker, 1974; Stryker & Sherk, 1975), this failure to replicate is by no means universal (Turket, Gijsbers, & Pritchard, 1975).

The plastic effects observed in kitten visual system have commonly been attributed to the rapid neural growth which is taking place in the nervous system during early development. The term "critical period" has been applied to this early period of heightened susceptibility of neural organization to environmental influence (Hubel & Wiesel, 1970). After the "critical period" when the pattern of synaptic contacts is established, however, the visual system is relatively immune to insults such as monocular deprivation (Wiesel & Hubel, 1963a, 1965; Hubel & Wiesel, 1970).

Plasticity in the Adult Visual System

Although neurophysiological investigations have yielded consistently negative results regarding plasticity

in the adult visual system (Wiesel & Hubel, 1963a, 1965; Hubel & Wiesel, 1970), there is considerable evidence to suggest that visual plasticity does occur in adults, at least at the perceptual level. Experiments where subjects were required to wear inverting prisms have shown that after a few weeks of experience adaptation takes place (Stratton, 1896, 1897; Peterson & Peterson, 1938; Snyder & Pronko, 1952). Kohler (1951, 1953, 1964; cited by Kling and Riggs, 1971) reported that after an extended period subjects achieve impressions which were "correct." In another line of research Julesz (1974) has studied retinal disparities which are never used in normal vision. He increased disparities in a random dot stereogram and presented them tachistoscopically to prevent convergence. He reported that after a large number of trials, many subjects began to see depth in the stereograms. These results suggest that some plasticity could occur at the underlying neural level as well.

Only recently Creutzfeldt and Heggelund (1975) have reported plastic changes in the adult cat visual system which they feel may be related to perceptual aftereffects. Using a paradigm similar to the rearing procedure of Blakemore and Cooper (1970), adult cats were exposed to vertical stripes for 1 hr. a day over a period of two weeks. At all other times they were kept in the dark. This procedure produced a decrease in the number of cells

and number of columns of cells which responded to vertical stimuli. This effect is different from that reported in kittens for a number of reasons. First, a decreased, rather than an increased sensitivity to the adapting stimulus was reported. Secondly, the effects were not presumed to be permanent.

Recently, evidence has also been obtained for plasticity of a more enduring nature in the adult visual system following chronic monocular paralysis. Buchtel, Burlucchi, & Mascetti (1972) found behavioral deficits in monocularly paralyzed adult cats which could not be accounted for on the basis of optical malfunctions. They also found a decrease in the number of cortical cells which could be driven by both eyes (3/10 vs. 8/10 in normal animals).

In a more detailed physiological analysis of the effects of monocular paralysis on adult cats, Fiorentini and Maffei (1974) studied cortical cells whose receptive fields were located within 5° of the area centralis. They found that long-term monocular paralysis produced substantial changes in the ocular dominance distribution of simple cells in visual cortex while that of complex cells was apparently unaffected. For the first week after monocular paralysis they found that a very high percentage of both simple and complex cells were binocular. These percentages were consistent with those reported for the

normal cat. After 8 days or more of monocular paralysis, however, they recorded an abnormally small percentage (15%) of binocular simple cells, while the percentage of binocular complex cells remained normal. Furthermore, this loss of binocularity in simple cells occurred rather suddenly about the seventh or eighth day of the paralysis and remained unaltered over several months regardless of any recovery of oculomotricity.

This type of neural plasticity in the adult is highly significant both theoretically and clinically. This adult neural plasticity may provide a basis for the understanding of the neural substrates of the perceptual plasticity seen in adult humans. Secondly, findings such as those of Fiorentini and Maffei (1974) may lead to a rejection of the current notions of the morphological bases of plasticity reported in the kitten visual system and its age-related limits. Certainly the changes reported by Fiorentini and Maffei (1974) are not the product of rapid neural growth or development. They occur in an adult nervous system long after morphological development is complete. Finally, as Fiorentini and Maffei (1974) point out, the rapidity of the changes observed in cat cortex have implications for the treatment of paralytic strabismus. It would seem fruitful, then, to investigate more fully the effects of chronic eye immobilization on the adult visual system.

Purpose of the Present Study

Research on immature nervous systems, as indicated earlier, has demonstrated plasticity at subcortical levels, including the dorsal lateral geniculate nucleus, in addition to the changes in cortex. This suggests that monocular paralysis in adult cats could produce subcortical effects in addition to the cortical changes. Further, the specific nature of the changes in the lateral geniculate might be predictable in terms of the parallel processing model of connectivity within the geniculostriate system (Stone, 1972). This model employs the X/Y distinction of retinal ganglion and lateral geniculate cells discussed earlier. In the parallel processing model X-cells and Y-cells constitute two distinct pathways which independently convey visual information to the visual cortex. The axons of X-type retinal ganglion cells contact X-cells in the LGNd which then contact primarily simple cells in the visual cortex. The Y-cells in the lateral geniculate receive input from Y-cells in retina and contact complex cells directly without first synapsing on simple cells. The parallel processing model, therefore, would predict that if, as Fiorentini and Maffei reported, simple cortical cells are affected selectively by monocular paralysis, any effect that is seen in the lateral geniculate should be confined to the X-cell population.

In the following experiment, therefore, the effects of monocular paralysis on the X- and Y-cell population of the dorsal lateral geniculate nucleus (LGNd) of the adult cat were studied.

CHAPTER II

METHOD

Subjects

Ten adult mongrel cats, weighing between 2.0 and 3.5 kg, were obtained from a local source. They were quarantined, housed and maintained on ad lib. food and water as required by FDA regulations during the course of the experiment. Antibiotic therapy and dietary supplements were administered as required by individual subjects. After physiological data had been obtained, subjects were sacrificed. The brain was perfused and extracted for histological verification.

Surgical Preparation

Unilateral eye immobilization was produced by transection of cranial nerves III, IV and VI at the point of their common entry into the orbit. In this preparation a ventral approach was used. This approach is similar to that frequently used in optic chiasm section in the cat (Myers, 1955; Trevarthen, 1972).

Each subject was tranquilized with acepromazine maleate and anesthetized with sodium pentobarbital. The animal's head was then placed in the stereotaxic in the normal position and rotated 180° so that it assumed the

position recommended by Trevarthen (1972) for a ventral approach to optic chiasm section. The lower jaw and tongue were retracted, exposing the roof of the mouth. An incision, 1.5 to 2.0 cm in length, was then made on the midline of the soft palate beginning just posterior (2-3 mm) to the hard palate. Infusion of this area with epinephrine hydrochloride prior to the incision controlled bleeding. After hemostasis was achieved by direct pressure, the sides of the incision were retracted to expose the roof of the nasopharynx. The mucosa of the nasopharynx was then excised, exposing the ventral aspect of the presphenoid bone. Figure 1 shows the portion of the skull exposed by this procedure. The transverse suture (marked by A), which separates the presphenoid and basisphenoid bones, marks the caudal limit of the optic chiasm.

The ventral portion of the presphenoid was then removed with a medium-sized dental burr. Drilling was begun in the anterior portion of the nasopharynx and extended laterally and caudally. In this area of the skull there is a thin layer of bone overlaying an air sinus (sphenoid sinus) and the dorsal portion of the presphenoid which encases the optic nerve, optic chiasm, and optic tract. Drilling was continued until these structures, still encased in bone, could be visualized. Cranial nerves III, IV and VI are encased in a heavily vascular bundle which also contains the anterior carotid artery and

THE SKULL, VENTRAL VIEW

1 basisphenoid bone
2 canal for Eustachian tube
3 canine tooth
4 external auditory meatus
5 first premolar
6 foramen magnum
7 foramen ovale
8 foramen rotundum
9 frontal bone
10 hamulus of pterygoid process
11 hypoglossal foramen
12 incisive foramen
13 incisors
14 infraorbital foramen
15 internal nares
16 jugular foramen
17 jugular process
18 malar bone
19 mandibular fossa
20 mastoid process of temporal bone
21 molar tooth
22 occipital bone
23 occipital condyle
24 palatine bone
25 palatine process of maxilla
26 palatine process of premaxilla
27 posterior palatine foramen
28 postorbital process of malar
29 presphenoid bone
30 pterygoid process of basisphenoid
31 styliform process
32 stylomastoid foramen
33 tympanic bulla
34 third premolar
35 vomer
36 zygomatic process of maxilla
37 zygomatic process of temporal

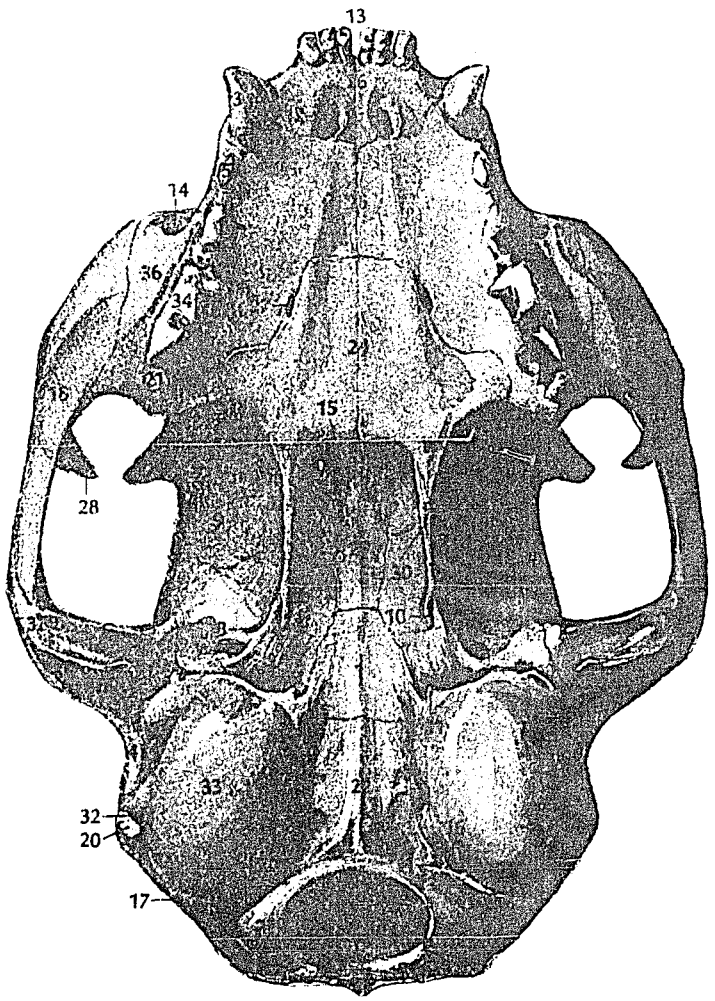
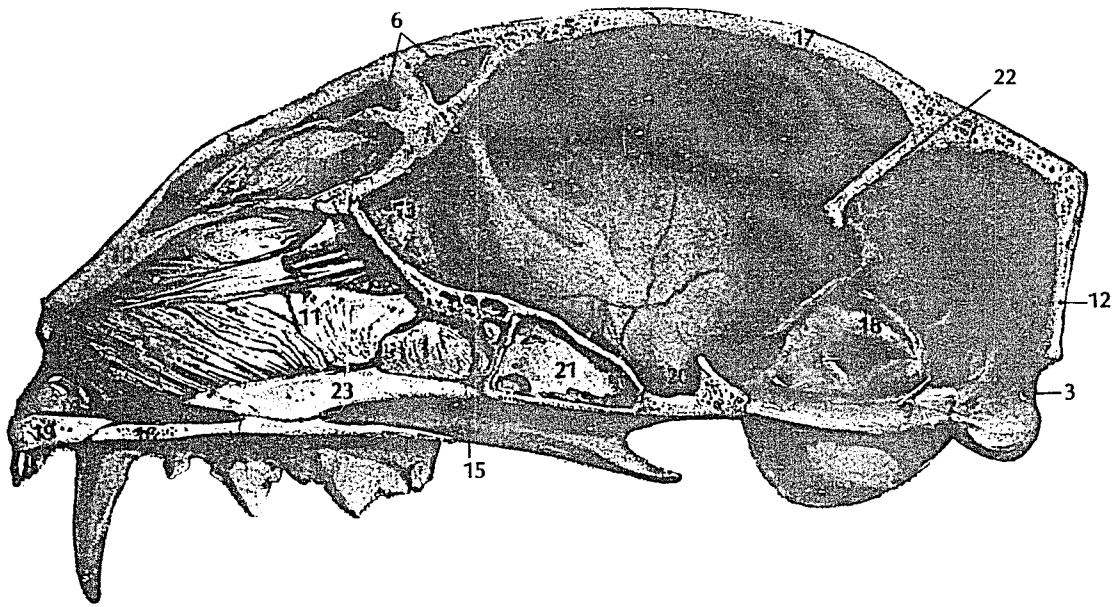


Fig. 1. The Skull, Ventral View. Area enclosed by rectangle is that exposed in surgical preparation (Diagram from Gilbert, 1968).

cavernous sinus. It is lateral and ventral to the lateral extent of the optic chiasm. At this point in the preparation this bundle remained encased in bone. Figure 2 shows the location of this bundle with respect to relevant landmarks.

At this point the actual exposure of the vascular bundle was begun. Just lateral to the optic chiasm the bone encasing the optic nerve and tract forms a dimple which extends laterally. Using a small, sharp dental burr, the ventral aspect of this dimple was removed for a distance of 2-3 mm. Care was taken to leave intact the final layer of bone which overlays the visual structures. Drilling was continued laterally until this entire shelf was removed, a distance of about 3-5 mm. Since bleeding was usually profuse during this procedure, gelfoam and aspiration were used to achieve hemostasis. After this bottom ledge had been removed, exposure of the more ventral portions of the vascular bundle was begun. Bone was cleared from the medial surface of the bundle, across the top and continued laterally until the entire vascular bundle was free of bone for a distance of about 5 mm in the anterior-posterior direction.

In this procedure the entire vascular bundle and all cranial nerves were cut without dissection. After the vascular bundle was clear of bone, it was clamped with a straight hemostat. Using sharp iris scissors, the first cut



SAGITTAL SECTION OF THE SKULL

1	cerebellar fossa	10	nasal bone	18	petrous part of petromastoid
2	cerebral fossa	11	nasal conchae	19	premaxilla
3	condyloid canal	12	occipital bone	20	sella turcica of basisphenoid
4	cribriform plate of ethmoid	13	olfactory fossa	21	sphenoidal sinus of presphenoid
5	frontal bone	14	optic foramen	22	tentorium
6	frontal sinuses	15	palatine bone	23	vomer
7	hypoglossal foramen	16	palatine process of maxilla		
8	internal auditory meatus	17	parietal bone		
9	jugular foramen				

Fig. 2. Sagittal Section of the Skull. Nerves lie just lateral to sphenoidal sinus #21.

was made posterior to the position of the hemostats. After hemostatis was achieved, a second cut was made anterior to the hemostats. In this manner a section of nerves about 2-3 mm in length could be removed. This area was then packed with gelfoam and topical antibiotics. The effectiveness of this resection was then assessed by examination of the pupil for signs of constriction. A final assessment for extraocular motricity could not be made, however, until the subject had recovered from the surgery.

During the same surgical procedure, subjects were also prepared for semichronic microelectrode recording after the method described by Orem, Schlag-Rey and Schlag (1973). After transection of cranial nerves III, IV, and VI, the subject was again rotated in the stereotaxic so that it assumed the normal upright position. In this procedure the skull was exposed and cleaned. A craniotomy, 4 by 5 mm, was then performed over the LGNd contralateral to the immobilized eye. The exact atlas (Snider & Niemer, 1961) coordinates that were used were anterior 3.0-8.0, lateral 8.0-12.0. Care was taken to insure that the meninges remained intact until recording. This hole was then sealed with bone wax until recording sessions. During this same preparation three bolts were imbedded in a pedestal of dental acrylic so that the head of the subject would be fixed in the stereotaxic plane during recording. This

pedestal was attached to the skull by inversely mounted skull screws which were also imbedded in the acrylic.

Apparatus

Action potentials of units from layers of the LGNd which were driven by the immobilized eye were recorded with Frederick Haer & Co. #20-10-1 stainless steel microelectrodes insulated with Epoxylite. The tip diameters of these electrodes were approximately 1μ and they had a tip impedence of 10-20 megohms measured at 1000 Hz.

The signal from these microelectrodes was amplified on a WPI Dam 5 preamplifier and Grass AC Amplifier. This output was displayed on a Hewlit Packard 141A Storage Oscilloscope and monitored through an audiomonitor. It was also recorded for subsequent analysis on magnetic tape including integration on a Grass Wide Band AC Integrator.

Procedure

General recording procedures. During recording sessions subjects were sedated, but not anesthetized, with a mixture of acepromazine maleate and sodium pentobarbital. They were restrained and their heads fixed in the stereotaxic plane by means of the chronically implanted bolts attached to a metal mount (Orem, Schlag-Rey, & Schlag, 1973). No general paralysis was induced since only cells driven by the surgically immobilized eye were under investigation. The eyes were protected by plano-contact

lenses and refracted with spectacle lenses so that sharp focus was obtained on a white tangent screen 1 m from the cat's eye. Lenses of varying refractive index were applied and black targets used to determine the appropriateness of each lense. The eye of the subject was considered to be in sharp focus when cells in the central visual field responded to a 1/4° dark target moved through their receptive field position on the tangent screen. The optic disk and area centralis were located on the tangent screen after the method of Fernald and Chase (1971). In this procedure retinal landmarks were located using an ophthalamoscope and the reflection projected onto the tangent screen and marked. Receptive fields were located and mapped with respect to these retinal landmarks using small dark targets.

All experimental sessions were run with the room lights on, an illumination condition which is in the high mesopic range for the cat. The reflectance of the tangent screen was measured at 1.8 log ft. lamberts.

Each recording session lasted about 7 to 8 hours and cats were allowed to recover completely before further recording. Subsequent recording sessions were run at intervals of two to three days.

Standard Horsley-Clarke procedures were used to place electrodes in the LGNd contralateral to the immobilized eye. Immediately before each penetration the menninges were reflected at the point of the penetration. Identification of recordings as originating from geniculate cells

was based on the criteria of Bishop, Burke and Davis (1962) and Hubel (1960). Histological verification and track reconstruction were done for selected penetrations after animals had been sacrificed.

In order to assure the randomness of the cell sample, all penetrations were made in the vertical plane. After each penetration the electrode was moved at least .2 mm in one direction. No two passes were made at the same atlas coordinates in a single cat. The same region of LGNd was sampled in each cat, however, to eliminate any variability which could have resulted from differences in the distribution of X- and Y-cells at different retinal eccentricities.

Because the results described by Fiorentini and Maffei (1974) were limited to cells whose receptive fields fell within 5° of the area centralis, this experiment focused primarily on units whose receptive fields were located in the central area of visual space. Some cells in more peripheral areas were sampled, but only those in the binocular segment were included in this experiment.

Classification of LGNd units. Units in the layers of the lateral geniculate nucleus which were driven by the immobilized eye were classified as X-cells or Y-cells on the basis of standard tests which have been described by previous authors. The tests which were used and the responses of each class of cell are discussed below.

1) Responses to a radial grating (Dubin, 1974; Cleland, Levick, & Sanderson, 1973). These tests employed a circular target which could be rotated about its point of symmetry. The grating used in this experiment subtended a visual angle of 9° at a distance of 1 m and was divided into eight equal black and white (contrast 80%) sectors. A neutral center, subtending 2° of visual angle, was used to mask the center of the cell's receptive field. When this target was centered on the cell's receptive field and rotated with a rapid jerky movement, Y-cells responded to this target with a brief excitation (Cleland, Levick, & Sanderson, 1973). When the target was centered and rotated at a steady rate of 40 rpm, Y-cells showed a modulated response and frequently an overall increase in response rate (Dubin, 1974). X-cells did not respond to any type of concentric rotation of this target, only to its movement through the receptive field.

2) Responses to flicker stimulation (Fukada, 1971; Fukada & Saito, 1971). In these tests the eye was stimulated with brief flashes of light from a Xenon arc photostimulator at flash frequencies which ranged from 1 to 60 Hz. Y-cells responded to this stimulus with an increase and then decrease of mean impulse density as the flash frequency was increased. They also continued to emit rhythmic bursts of spikes for an extended period after the flash train was terminated. X-cells, however, showed an

unchanged spike rate over a wide range of flash frequencies and quickly returned to their base firing rate after the termination of the train.

3) Responses to moving targets (Cleland, Dubin, & Levick, 1971). This test employed a large (4°), black target which was fixed to the end of a thin wire. Y-cells responded to the movement of this target through their receptive fields, regardless of the velocity of movement. X-cells, however, failed to respond to fast movements provided the target was larger than the center of their field.

4) Responses to moving square wave gratings (Enroth-Cugell & Robson, 1966; Cleland, Dubin, & Levick, 1971; Hoffmann, Stone, & Sherman, 1972). These tests employed a series of square wave gratings consisting of equally spaced black and white (contrast 80%) stripes with spatial frequencies of 1, 4, and 6 cycles per degree. When these gratings were moved slowly (2-3 degrees per second) through the cell's receptive field, X-cells responded with a modulation of the maintained discharge rate about their mean level for all spatial frequencies. As finer gratings (4-6 cycles per degree) were used, however, Y-cells failed to modulate and instead showed an unmodulated increase in their mean discharge rate (Enroth-Cugell & Robson, 1966; Cleland, Dubin, & Levick, 1971). When the rate at which a coarse grating (1 cycle per degree or less)

was moved through the cell's receptive field was varied, characteristic responses were also obtained. X-cells responded by modulating to each cycle of the grating although this response sometimes grew progressively weaker as the rate was increased. At very high velocities (25 degrees per second or greater) X-cells did not respond to this grating at all as long as the edge did not cross the cell's receptive field. Y-cells, however, responded with a burst of spikes which lasted through several cycles of movement.

These tests were generally in good agreement with each other concerning the classification of units as X or Y. For some cells, however, one or more of the tests failed to produce conclusive results. These findings are consistent with other research concerning LGNd cells (Hoffmann, Stone, & Sherman, 1972). In this experiment the radial grating test suggested by Dubin (1974) was used as the primary diagnostic tool because it appeared to give the most definitive identifications.

Assessment of reliability of classification. In order to assess the reliability of the judgments which resulted in a cell being classified as X or Y, several procedures were employed. First, during recording sessions multiple observers were used to arrive at a judgment independently. At all times there were at least two and

usually three observers making judgments. In addition, each test was repeated several times on each cell unless the cell was lost before the repetitions were possible. Examples of the few cells causing disagreement are discussed in the results chapter.

In addition to these procedures which were employed during recording sessions, cells were reclassified from the taped and integrated recordings several weeks after the experiment was completed. The observer making these judgments had no knowledge of the original classification of the cell or the condition in which it was recorded. These classifications were then compared to those judgments made during the recording sessions. Again, cases in which disagreement arose are discussed in the results section.

Comparison of acute and chronic monocular paralysis. In the first phase of this experiment, the effects of chronic eye paralysis on the LGNd were assessed by comparing the relative proportion of X- and Y-cells which were recorded either a short time or a long time after surgery. Recordings were made at either 1 to 3 days following surgical eye immobilization (acute condition) or at more than 14 days (chronic condition). These intervals were chosen to place these observations clearly on either side of the 7- to 8-day period reported to be

critical for the observation of the cortical effect of monocular paralysis. The acute condition served as the control condition since the 1- to 3-day period is far shorter than that reported to be necessary for the appearance of the cortical effect and presumably any effect in the LGNd as well. Different animals were run in each group to eliminate any bias which could have resulted from sequential recording in a single animal.

Longitudinal observations. This phase of the experiment dealt with the time course of the effect within individual cats. Subjects were run repeatedly at intervals of two to three days beginning in the acute (one to three days) period until they showed a progression to chronic proportions of X- and Y-cells. All recordings in these animals were limited to the central 10° of the visual world to eliminate any bias which resulted from retinal eccentricity.

CHAPTER III

RESULTS

Behavioral Observations

During the course of this experiment no formal investigations were performed to assess possible visual deficits following chronic monocular paralysis. Subjects were closely observed, however, as they moved freely about the laboratory and colony rooms.

Immediately following surgery subjects were ataxic and lethargic. By the day following surgery, however, these symptoms had usually disappeared and most subjects had begun to eat and drink, at least in limited quantities. In general, subjects did not exhibit any gross deficits in visually guided behavior at any time following the surgical paralysis. With both eyes open, they appeared able to fixate and track objects normally. They were also able to jump up or down from ledges quite accurately and without hesitation.

Shortly following surgery, however, most subjects were observed to adopt an unusual posture when fixating or tracking objects. They tilted their heads such that the mobile eye seemed centered on the object. They also appeared to use head movements, rather than eye movements, to follow an object. This tendency gradually dissipated, however, and was not noticeable by two weeks following surgery.

On only one occasion an animal was observed while its mobile eye was occluded and its immobile eye fitted with a 2 mm artificial pupil. The subject was able to track moving objects and would turn its head to fixate small moving objects placed in its peripheral field of vision. With respect to stationary objects, however, the animal appeared almost blind. It bumped into furniture and even walls as it moved around the room. During this session the subject did not appear to use head movements to compensate for this visual deficit. This was the subject's first experience with occlusion of the mobile eye, however, and this response may have appeared with additional exposure.

Single Unit Recordings

Classification of units. During the course of this experiment recordings were made from 273 units. Of these 257 (94%) were classified as X-cells or Y-cells on the basis of the standard visual tests discussed in the methods chapter. The remaining 16 units which were not classified as X-cells or Y-cells fell into two groups which have been characterized as "ambiguous" (neither clearly X- nor Y-cells) and "unclassifiable" cells. The properties of these two types will be discussed later.

After application of the reliability measures discussed in the methods section, 257 units were classified as X-cells or Y-cells. These units gave differential responses to a number of visual stimuli. Figure 3 illustrates

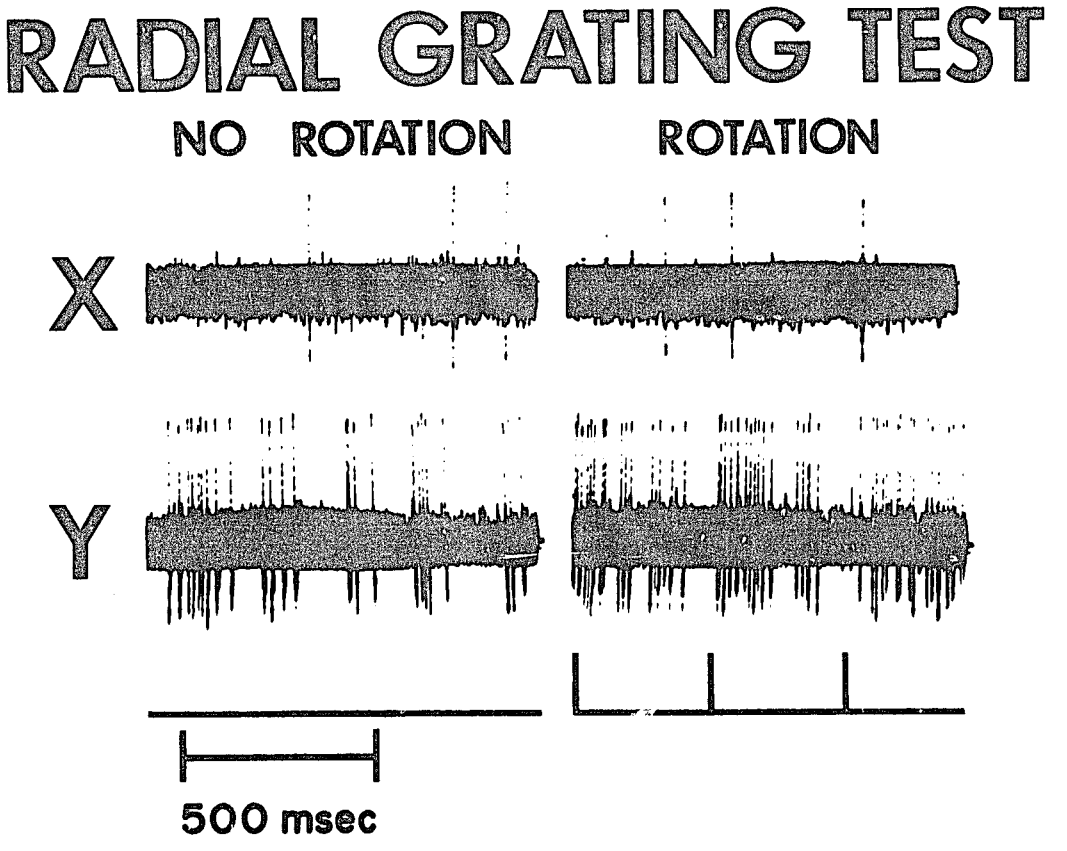


Figure 3. Spike records of a typical X-cell (X) and a typical Y-cell (Y) to rotation of a radial grating at 45 rpm. The first trace in each pair shows the cells' base firing rate when the grating is centered on the receptive field without rotation. The second trace in each pair shows the cells' responses to rotation. The stimulus mark indicates one cycle of the grating crossing a specified point.

characteristic responses to the radial grating test of Dubin (1974) which was used as the primary diagnostic tool. The first trace in each line illustrates the firing pattern of each cell when the stimulus was centered on that cell's receptive field without rotation. The second trace illustrates the cell's response to rotation of the radial grating. Fig. 3X shows the spike record of an X-cell's response. It can easily be seen that there is no difference between the cell's overall firing rate or distribution of spikes between the first and second trace. In contrast, Fig. 3Y illustrates the response of a typical Y-cell. It can be seen that the cell both increases its overall rate of firing and shows a modulated discharge in response to the rotation of the grating.

Aside from the responses to the radial grating, another characteristic of X- and Y-cells is evident from these traces. The X-cell has a much lower base firing rate (3 spikes per second) than the Y-cell (25 spikes per second). In general, this tended to be the case although some exceptions were found.

Figure 4 illustrates the integrated records of typical X- and Y-cells' responses to some of the other stimuli used to classify cells. The traces in Fig. 4a show the responses of an X-cell and a Y-cell to flicker stimulation. The X-cell shows an unchanged spike rate over a wide range of flash frequencies and a rapid return to its base rate after termination of the train. The Y-cell, however, shows

a maximum response to stimulation of about 20 Hz. The Y-cell also continues to emit rhythmic bursts of spikes after the train has been terminated. Fig. 4 b) and 4 c) illustrate the responses of an X-cell and a Y-cell to the movement of a square wave grating. The first trace in each pair shows that all cells respond similarly to slow movement of a coarse grating. The second trace, however, shows the characteristic responses which are obtained when the rate of movement (Fig. 4 b) or the spatial frequency (Fig. 4 c) of the grating is increased. In both cases Y-cells respond with an unmodulated increase in their mean discharge rate. X-cells, however, do not respond to the fast movement of the coarse grating (Fig. 4 b) and continue to modulate without any increase in rate to the fine grating (Fig. 4 c).

Sixteen units were not classified as X- or Y-cells because their responses were not sufficiently characteristic of one group or the other. Nine of these units were characterized as "unclassifiable" and all of these exhibited similar receptive field properties. These units lacked the well-defined receptive field center which is characteristic of LGNd cells. In addition, they were only weakly responsive to photic stimulation and did not respond to any of the targets used in this experiment to classify cells. Generally, it was impossible to localize a receptive field for any of these cells with confidence.

Cells with these response properties have been reported in the cat LGNd by Hoffmann, Stone and Sherman (1972) but were excluded from their analysis because they did not show properties of either X- or Y-cells.

The remaining 7 of the 16 units which were not classified were characterized as "ambiguous." These cells had well defined receptive field centers and other characteristics typical of LGNd cells but they could not be classified as X- or Y-cells with confidence based on their responses to visual stimuli. Lack of confidence was recognized when discrepancies arose in the way a cell was classified during one or more of the reliability procedures; that is, when there was disagreement between observers, or between tests during recording sessions or between the judgments made during the session and later. In retrospect it was found that cells which failed one reliability procedure often tended to fail them all. The responses of these cells to the radial grating tended to fall into two groups. Figure 5 illustrates the integrated responses of a typical X-cell, a typical Y-cell, and two ambiguous cells to rotation of the radial grating. The first trace in each pair shows each cell's integrated spike rate when the stimulus was centered on the receptive field without rotation. The second portion of the trace shows the

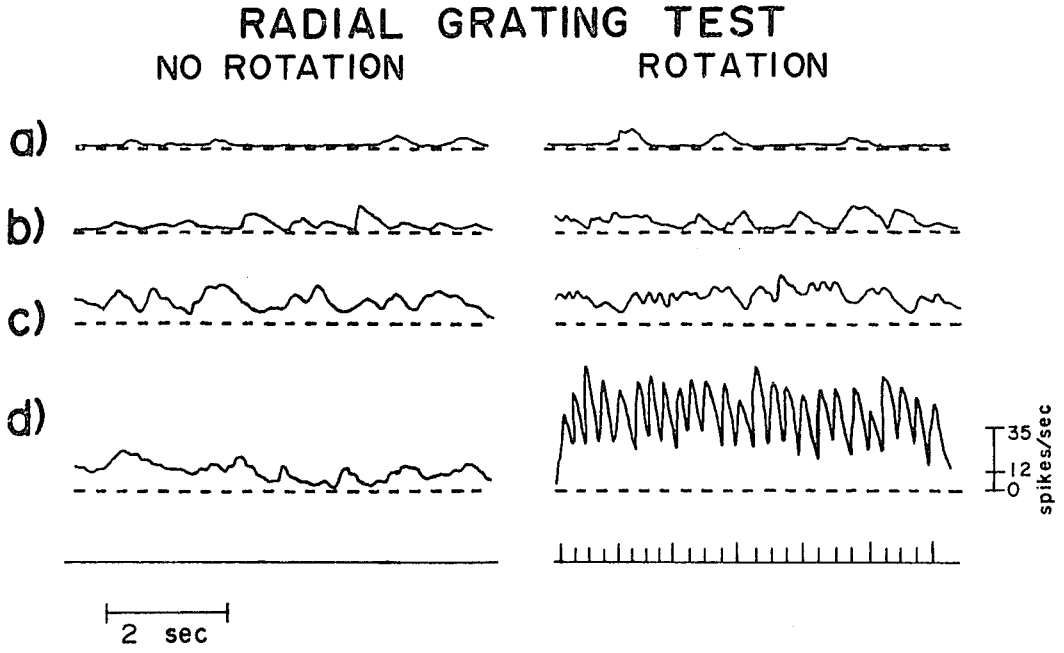


Figure 5. Responses (integrated records) of an X-cell, two ambiguous cells, and a Y-cell to the radial grating. a) typical X-cell. b) a cell with some X-cell characteristics but some increase in response rate during the rotation of the grating. c) a cell with some Y-cell characteristics but a weak and transient modulated response. d) typical Y-cell.

cells' response to the rotation of the grating. As illustrated in Figure 3 the X-cell (Fig. 5 a) and the Y-cell (Fig. 5 d) give clearly definitive responses to the rotation of the grating. Such is not the case, however, with the ambiguous cells (Fig. 5 b and 5 c). The cell in Fig. 5 b shows a low base firing rate, similar to the X-cell. It shows a slight, unmodulated increase in rate, however, during the rotation of the grating. In contrast, the cell in Fig. 5 c shows many of the response properties of a Y-cell such as a high base rate of firing. During the rotation of the grating, however, it exhibits very weak modulation. Its increase in overall rate of firing is also increased only slightly, if at all.

Both the unclassifiable cells and the ambiguous cells occurred with roughly equal frequency in all conditions (acute, chronic and intermediate states). It seems highly unlikely, therefore, that their occurrence represented any significant trend in the data. Furthermore, they occur with such low frequency that their inclusion in any analysis would have little influence on the conclusions of the experiment. For these reasons, therefore, they have been excluded from all additional analyses and shall not be mentioned further.

A comparison of proportions of X- and Y-cells recorded in the acute condition with previously reported

data As mentioned in the Methods Chapter, cells recorded in the acute condition (1-3 days of monocular paralysis) in this experiment served as comparison data for assessing the effects of monocular paralysis. Before discussing the effects of chronic monocular paralysis with respect to these data, however, it is first necessary to compare these acutely recorded data with those obtained by previous investigators to demonstrate that differences in techniques cannot explain any effects observed. To date, the most extensive investigation of the X- and Y-cell populations of the LGNd has been conducted by Hoffmann, Stone and Sherman (1972). The acute data collected in this experiment, therefore, have been compared to those reported by Hoffmann, Stone and Sherman (1972).

Of the 49 cells recorded in the acute condition of this experiment, 45 (90%) were classified as X-cells or Y-cells. Of these 22 (49%) were classified as X-cells while 23 (51%) were classified as Y-cells. These results are in good agreement with those of Hoffmann, Stone and Sherman (1972) who report 50% X-cells and 50% Y-cells for the entire binocular segment of the cat LGNd.

Table 1 summarizes the proportions of X-cells and Y-cells recorded in this experiment and by Hoffmann,

Table 1

Comparison of Proportions of X- and Y-Cells in Acute Condition with Previously Reported Data (Hoffmann, Stone, & Sherman, 1972)

	Hoffmann, Stone, & Sherman			Acute Data			Net Diff.(%)
Receptive Field Location	# Cells	%X	%Y	# Cells	%X	%Y	
Total Bin. Seg.	245	50%	50%	45	49%	51%	-1%
0 -10°	109	58%	42%	25	56%	44%	-2%
10°-20°	49	45%	55%	10	40%	60%	-5%
20°-M	87	40%	60%	10	40%	60%	0%

Stone and Sherman (1972) as a function of retinal eccentricity. Three categories of retinal eccentricity within the binocular segment have been employed: 0°-10° from the vertical meridian, 10°-20° from the vertical meridian, and 20° to the end of the binocular segment. Again, it can be seen that these figures are within a few percent in all categories. Most of these differences can probably be accounted for on the basis of the small number of cells sampled in this portion of the experiment. For the rest of this discussion, therefore, it will be assumed that cells recorded in the acute condition of this experiment constitute a normal sample which reflects a geniculate cell population comparable to that encountered by other investigators. By implication it follows that differences observed in the LGNd of chronically paralyzed animals arose from the eye paralysis and not differences in preparation or recording procedures.

Comparison of acute and chronic monocular paralysis. During the course of this experiment, 84 units were recorded in the chronic condition (16 days or more of monocular paralysis). Of these units 78 (94%) were classified as X-cells or Y-cells. There were no apparent differences in receptive field properties of X- and Y-cells recorded in the acute condition and in the chronic condition.

The proportions of X- and Y-cells recorded in the chronic condition, however, contrasted sharply with those recorded in the acute condition. After 16 days or more of monocular paralysis only 6% of the units encountered were X-cells, while the remaining 94% were Y-cells. These results are statistically significant ($\chi^2 = 27.8$, $p < .001$). Figure 6 summarizes the data obtained in both the chronic and acute conditions.

In Figure 7 the fraction of recorded units which were X-cells is displayed as a function of retinal eccentricity. The same categories of eccentricity have been used as in Table 1. It can be seen that the X-cell loss appears to be present in all areas of the binocular segment. The small sample size in the most peripheral areas, however, limits confidence with respect to the estimate of the magnitude of the loss in these areas.

Time course for the loss of X-cells. After establishing that there was a reduction in the proportion of X-cells recorded in the chronic (16 days or more of monocular paralysis) condition, the time course for this loss was studied. In order to minimize variability resulting from differential distributions of X- and Y-cells as a function of retinal eccentricity, only cells with receptive fields in the central 10° of visual space have been included in this analysis. Recordings have been grouped into 5

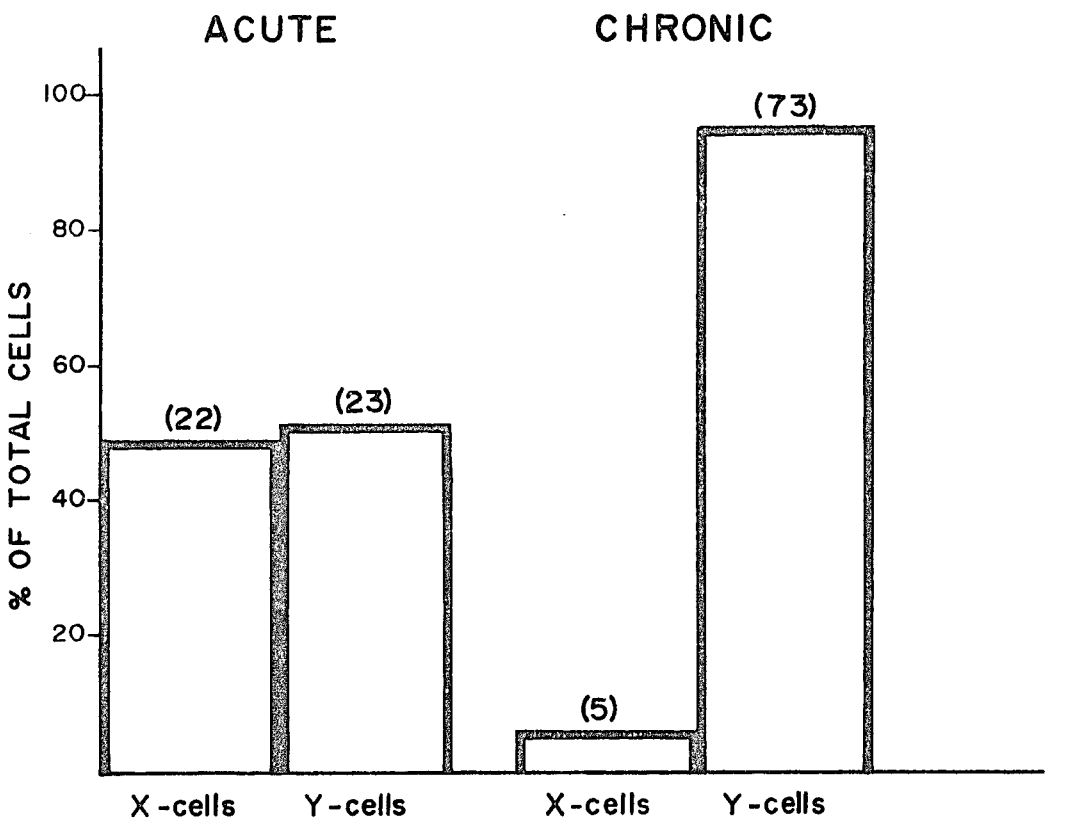


Figure 6. Proportions of X- and Y-cells recorded in the acute (0 to 3 days of paralysis) and chronic (16 days or more) conditions. The numbers in parentheses refer to the number of cells upon which the percentage is based.

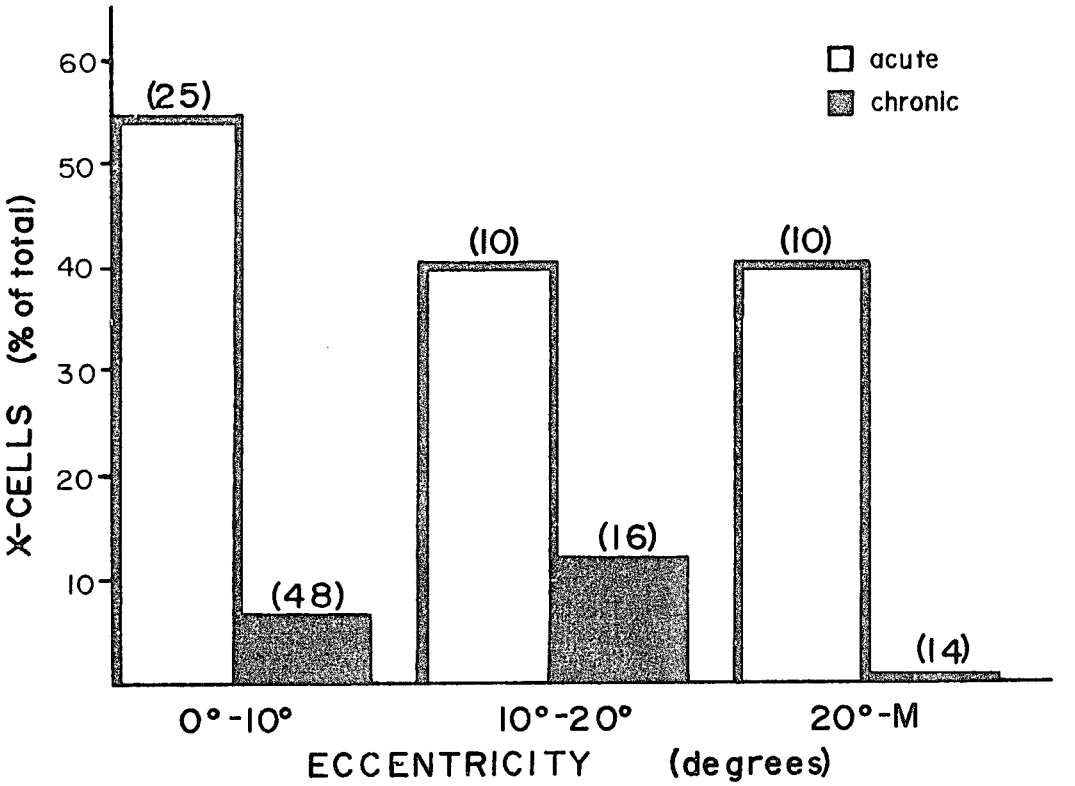


Figure 7. Proportions of X-cells recorded in the acute and chronic conditions expressed as a function of retinal eccentricity. Acute proportions are represented by open bars, chronic proportions are represented by dark bars. Three categories of retinal eccentricity are used: 0-10° from the vertical meridian, 10°-20° from the vertical meridian, and 20° to the end of the binocular segment(M). The numbers in parentheses refer to the number of cells on which the percentage is based.

periods of duration of paralysis: 0 to 3 days following surgery (this period corresponds to the acute condition), 4 to 7 days following surgery, 8 to 11 days following surgery, 12 to 15 days following surgery, and 16 days or more following surgery (this period corresponds to the chronic condition in the previous experiment).

Figure 8 summarizes the proportion of total units recorded which classified as X-cells in each of the five periods of duration of paralysis. As reported in the previous section, X-cells represent more than half (56%) of the total sample in the first three days following monocular paralysis. Following this acute phase, however, 36%, 28% and 27% X-cells were recorded for the 4- to 7-, 8- to 11-, and 12- to 15-day periods respectively. Finally, after day 16 only 6% of the cells recorded were X-cells. An overall statistical test showed that there was a significant difference between the percentages of X- and Y-cells recorded in these five groups ($\chi^2 = 22.8$, $p < .001$). Further analysis showed that there was no significant difference between the proportions of X- and Y-cells recorded in the 4- to 7-, 8- to 11-, and 12- to 15-day groups. Each of these groups, however, was different from the 0- to 3-day group ($\chi^2 = 11.8$, $p < .001$), and the 16- or more-day group ($\chi^2 = 11.0$, $p < .001$). Based on these data, then, the X-cell loss appears to occur

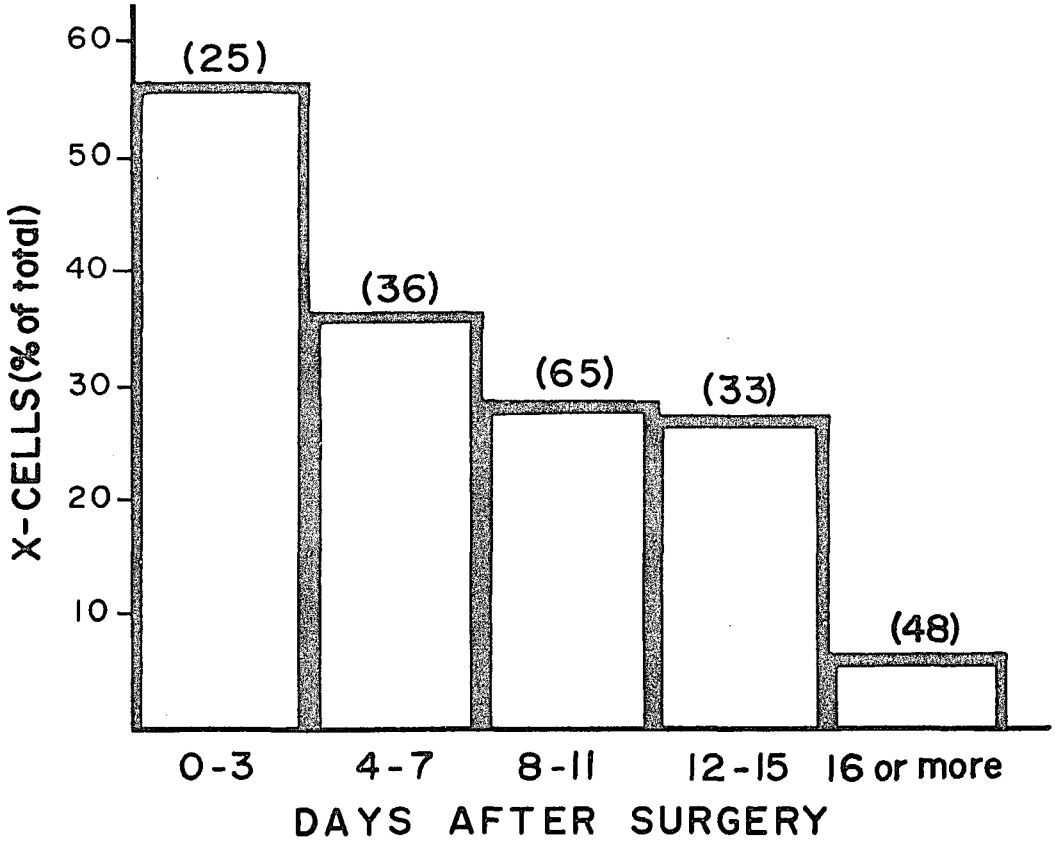


Figure 8. Proportion of total cells recorded which were X-cells as a function of duration of the paralysis. Five periods of duration were used: 0-3, 4-7, 8-11, 12-15, and 16 or more days of paralysis. The numbers in parentheses refer to the total number of cells recorded in each time period.

in two phases with two major points of reduction in the proportion of X-cells. One occurs around day 4 and the other around day 16.

Data from individual subjects. Figure 9 shows the proportion of X-cells from individual cats in each session as a function of the duration of the paralysis. Individual data points are represented by the closed points. Data points from the same subject are connected by lines. Several relationships emerge from this figure. First, there is a great deal of variability between the percentages recorded for individual cats on any given post-operative day. Part of this variability is undoubtedly due to the small number of units (usually between 5 and 15) sampled on any given day at this receptive field location. Part of the variability may also be due to differences in individual cats' responses to the surgical paralysis. At present, of course, it is not possible to specify how much of the variability is attributable to each of these sources.

Figure 9 also shows that, except for one cat who showed a slight increase in the proportion of X-cells from day 1 to day 3, all cats showed a decline in the proportion of X-cells recorded in subsequent sessions. Since subsequent sessions are necessarily recorded at a longer duration of paralysis than former ones, the result could be produced as a function of the increasing duration of paralysis. It

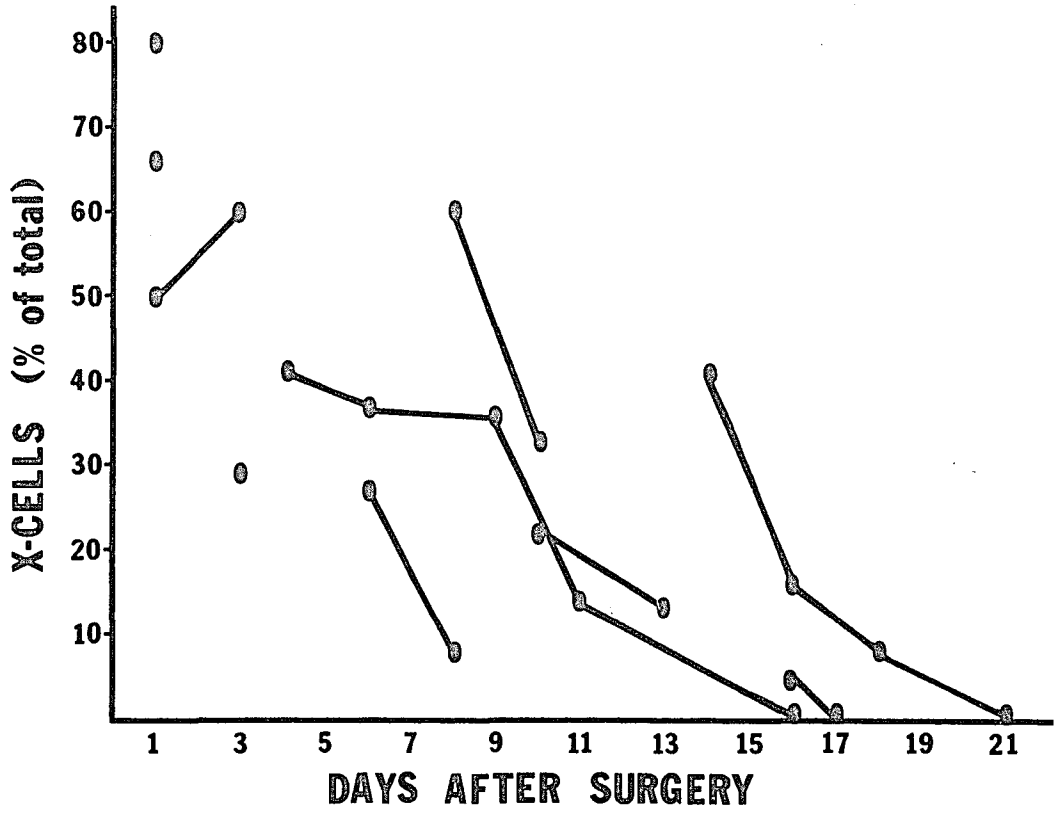


Figure 9. Proportion of cells which were X-cells recorded in each recording session expressed as a function of duration of paralysis. Data points from the same subject are connected by lines.

is also possible, however, that the observed declines were produced by the effects of sequential recording.

Assessment of the possible effects of sequential recording may be made by comparing Figures 9 and 10. Figure 10 shows the same data as Figure 9 replotted as a function of the number of recording sessions irrespective of the duration of the paralysis. Again, data points from subsequent sessions from the same cat are connected by solid lines. If the effects of sequential recording could account for the data of this experiment, Figure 10 should show two things. First, there should be a great deal less variability between data points collected in a given session than at a given duration of paralysis. This is obviously not the case as a comparison of Figures 9 and 10 shows. Secondly, lines connecting individual data points should have approximately the same slope. Again, this is clearly not the case. Some lines show a very sharp decline, while others show very little.

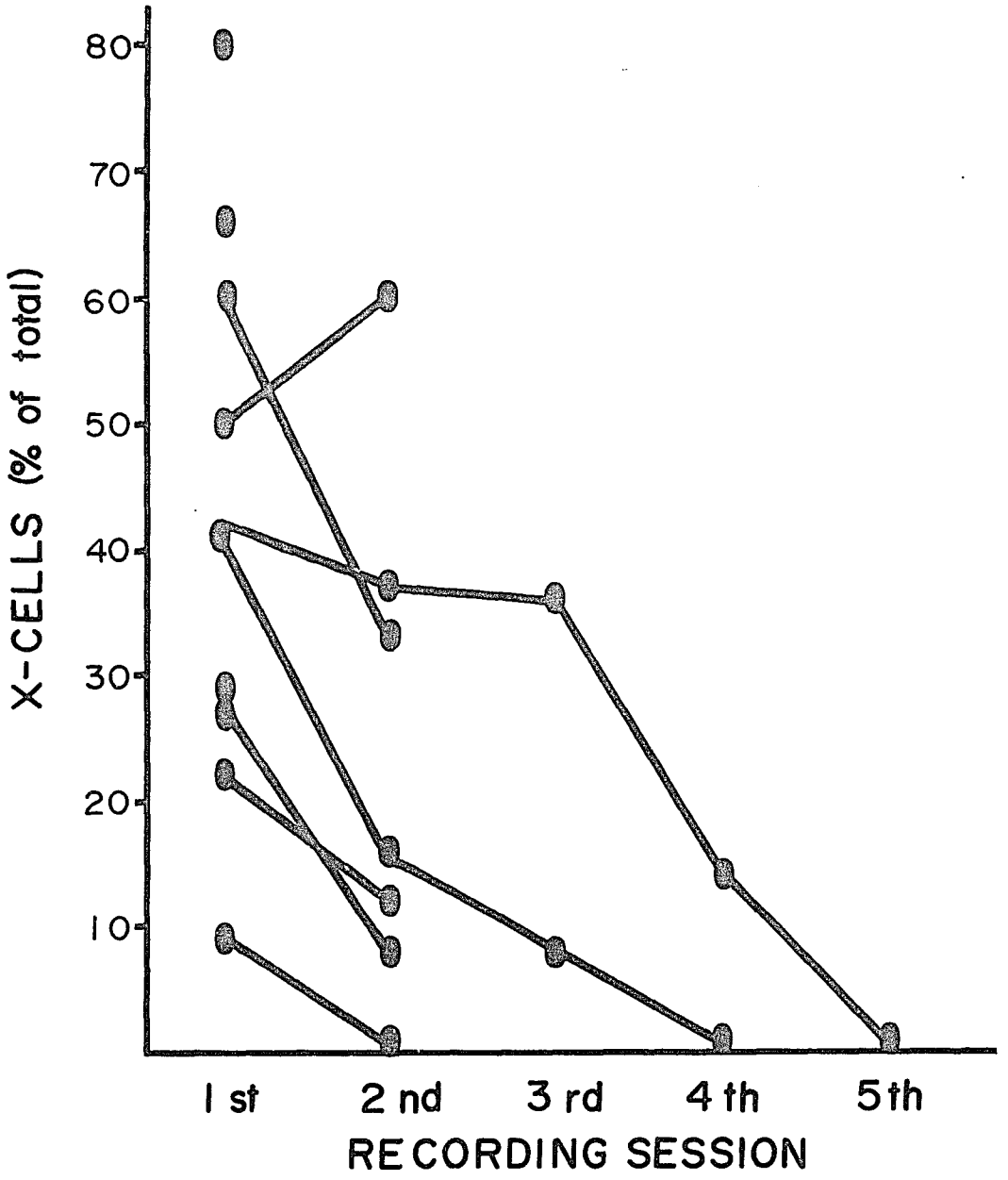


Figure 10. Proportion of cells which were X-cells recorded in each session irrespective of the duration of paralysis. Data points from the same subject are connected by lines.

CHAPTER IV

DISCUSSION

The results of this experiment illustrate a type of plasticity in the adult visual system heretofore unobserved. Following chronic monocular paralysis, the proportion of X-cells recorded in the LGNd of the adult cat was drastically reduced. Moreover, this change appears to be completed in a relatively brief period of time. Moreover, these findings have implications for a number of theoretical issues such as the validity of the X/Y distinction and models of information processing in the geniculostriate system. These issues are central to our understanding of how visual information is processed by the nervous system.

Before discussing in greater detail the implications of these results, however, a number of interpretative issues deserve discussion. Primarily, these issues concern the possibility of an artifactual result produced by the surgical procedure and the fate of the X-cells after chronic monocular paralysis.

Possible Artifacts of Surgical Monocular Paralysis

This experiment demonstrated a change in the rate of detection of X-cells in the LGNd of the adult cat following the surgical immobilization of one eye. Obviously, this

surgical procedure has severe consequences on the visual experience of the subject. The visual image at close ranges is severely degraded because accommodation is relaxed. Pupillary constriction is prevented, thereby altering depth of field and retinal illumination. Visual input from the two eyes is not coordinated in the normal manner because of the lack of ocular motoricity in the paralyzed eye. It would be desirable to infer that these factors in the subjects' visual experience produced the physiological effects. One might wish to argue, however, that the physiological effects found in this experiment were produced as an artifact of the surgical procedure itself, rather than by the stimulus consequences of the procedure. Although effects of this nature would be of interest and possible theoretical importance, they would not relate as clearly to the issue of environmental modification of neural structures.

Due to the surgical procedure, two possible sources of artifactual result are readily apparent. First, the surgical procedure could have produced damage to the optical structures or to the X-cells directly. A second possibility is that one or more of the drugs administered during the experiment produced the selective loss of X-cells. There was no control procedure (i.e. "sham" surgeries) in this experiment designed specifically to eliminate these possibilities, since both seem remote on logical grounds.

These possibilities, and the arguments against them, however, will be discussed in detail.

Any surgical preparation results in several obvious sources of trauma: damage produced by manipulation of the physiological structures, temperature loss due to exposure, or infection. While the possibility exists that the LGNd results were produced by surgical trauma, this possibility seems remote for several reasons. First, the optical structures (optic nerve, optic chiasm, and optic tract) were not directly exposed during the surgical resection of cranial nerves III, IV and VI. They remain encased in a layer of bone with the protective membranes intact. This greatly reduces the opportunities for trauma to be inflicted on these structures. Secondly, to explain the data reported in this experiment, any damage must not be immediately apparent, but only exert its effect over a period of more than two weeks. Furthermore, the damage must be selective for a single class of cells distributed across a large range of retinal eccentricities. These restrictions greatly reduce the possibilities for a traumatically-induced effect since most conceivable sources of damage would be immediately apparent upon recording or would not be selective for a single class of cells or their fibers. Finally, the brains of all subjects were perfused, extracted and examined after the recording was

completed. In no subject was there any sign of infection or other damage in the region of the visual structures.

There are two other, more subtle ways in which the surgical preparation may have produced an artifactual result through indirect trauma, however, One of these is through possible changes in intraocular pressure which could occur as a function of the surgical preparation. The other is through interruption of the venous drainage from the eye.

When cranial nerves III, IV, and VI were transected by the surgical preparation used in this experiment, a major portion of the venous system serving the eye was interrupted as well. One might wish to argue, then, the resulting decreased blood supply(and consequently oxygen supply) or the decreased vascular drainage could have produced the loss of X-cells reported in the LGNd. This possibility, however, seems unlikely for several reasons. First, as was the case with direct trauma, any effect due to this decreased circulation should produce a maximal effect on those areas of retina which were served by the interrupted vessels. This was definitely not the case in this experiment, as the effect was found to occur throughout the entire binocular segment. Secondly, it would be expected that any damage which resulted from circulatory disruption would be apparent very shortly after the surgery. Any long-term examination of the effects of circulatory

disruption should display recovery or at least no increased impairment. Finally, and most importantly, retinal landmarks including blood vessels were examined ophthalamologically during recording sessions and found to appear quite normal. It would seem that impairment in circulation sufficiently severe to produce a neurophysiological effect should be detectable in the appearance of vessels during this type of examination.

As mentioned previously, resection of cranial nerve III prevents pupillary constriction. This condition, at least in some species, results in the production of an acute open-angle glaucoma. This surgical procedure could produce an increase in intraocular pressure to which X-cells (presumably the smallest cells) in retina might be selectively sensitive. Although direct measurements of intraocular pressure were not made in this experiment, there are several reasons to believe that significant changes did not occur. First, the immobilized eye of each subject was examined daily during the course of the experiment for signs of residual oculomotricity and corneal degeneration. There were no signs of distention of the eyeball, as would be the case if intraocular pressure was severely increased. Secondly, as previously mentioned, retinal landmarks such as the optic disc and blood vessels were examined ophthalamologically during recording sessions. Changes in the appearance of these landmarks have been found to be very

sensitive indicators of intraocular pressure. At no time, however, were any abnormalities detected. Furthermore, Snodderly (1975) has made extensive measurements of intraocular pressure in monkeys following chronic monocular paralysis and found that no significant changes occurred at any time. It seems unlikely, therefore, that changes in intraocular pressure large enough to produce the results of this experiment occur in the cat following chronic eye immobilization. Finally, it must again be considered that the effects of chronic monocular paralysis are selective for a class of cells. Although experimentally induced glaucomas have been widely studied, there have been no reports of any such consequences. Thus, even if the surgical preparation had produced small changes in intraocular pressure, there still would be no reason to believe that these changes caused the X-cell loss.

Finally, there are two ways in which drugs could have produced the X-cell loss. First, one of the drugs administered during the surgical preparation could have produced the effect. Alternatively, one of the drugs administered during recording sessions could have, after repeated administrations, produced the effect.

When examining the possible effects of drugs which were administered only a single time, many of the same constraints which were considered above again apply. Namely, that the X-cell loss is only seen after a considerable

period of time, at least in relation to known drug effects, and it is selective for a single class of cells. Although the effects of all of the drugs employed in this experiment have been widely studied, there are no reports of effects on the nervous system such as those reported here. Furthermore, there is extensive clinical evidence concerning the effects of these drugs on human visual perception. No detrimental long term effects have ever been reported. To attribute the present results to drug effects, then, one must argue that there are species differences in the effects of these drugs, or that these drugs destroy the X-cell population of the LGNd in humans but that these cells have nothing to do with visual perception. Either of these arguments appears highly unlikely.

If the effects reported in this experiment were produced by one of the drugs administered during recording, sequential recording would be expected to greatly enhance the X-cell loss. As discussed in the results section, however, this does not appear to be the case. Despite the variability seen between subjects, there seems to be a far greater correlation between the percentage of X-cells recorded and the duration of the paralysis than between the percentage of X-cells recorded and the number of times from which an animal was recorded.

Nonvisual consequences of the monocular paralysis preparation, then, do not appear to be creditable sources

for the selective loss of X-cells reported here. The remainder of this discussion will therefore be based on the assumption that the effects of chronic monocular paralysis occurred as a consequence of the disturbances in visual input produced by the surgical preparation.

The Fate of the X-Cells

In this experiment there was a change in the percentage of X-cells detected following chronic monocular paralysis. As with any microelectrode study, however, it is not possible to determine the reasons for this failure to detect this class of cells. It appears that there are three possible explanations for the findings reported in this experiment.

The first, and preferred, explanation for the decrease in the percentage of detected X-cells following chronic monocular paralysis is that the X-cells in the LGNd are silent and nonfunctional. The X-cells in the LGNd may either be dead themselves, or deafferented. This explanation has major implications for a number of theoretical issues to be discussed later as well as for the issue of adult plasticity.

On the surface it may seem that this issue could be resolved by comparing the average number of cells recorded per pass in the acute condition with the average in the chronic condition. If one population (the X-cell population) were silent or missing in the chronic condition, it

would seem that there should be fewer total cells recorded per pass, particularly in the central areas of visual world where X-cells are normally the most frequently encountered. This was not the case, however. There were as many cells recorded per pass in the chronic condition as in the acute condition. This result, however, is not definitive to the issue. If the X-cell population is rendered nonfunctional through deafferentation, shrinkage is likely to occur. This condition, as well as cell death, would produce an increase in interstitial space. It is not unlikely that the remaining Y-cell population would expand to fill this space. Since the number of units recorded on any given pass is a small fraction of those present, the number of recorded units could remain unchanged even though one class was silent. The number of units recorded per pass, therefore, cannot be taken as definitive evidence against the nonfunctioning of the X-cell population.

A second explanation for the failure to detect X-cells is that they are both present and functional in the LGNd, but shrunken so that they were undetectable by the micro-electrodes used in this experiment. Such an explanation does not alter the basic conclusion of structural and functional plasticity in the adult visual system. It could, however, alter the theoretical implications of the results.

Without a detailed morphological study of the LGNd after chronic monocular paralysis, the possibility of cell shrinkage cannot be directly examined. Several lines of argument, however, suggest that shrinkage alone cannot account for the failure to detect X-cells. First, the major problem in obtaining recordings from small cells is the difficulty in isolating and keeping them until the experiment can be performed. If chronic monocular paralysis produced cell shrinkage in the LGNd, then a large proportion of the cells encountered in the chronic condition should have been lost during recording before the tests had been completed. This was definitely not the case in this experiment. Cells were no more difficult to isolate and hold in the chronic condition than in the acute. Even the few X-cells encountered in the chronic condition were as stable as in the acute. If cell shrinkage alone is used to account for the results of this experiment, then, it must be assumed that cells are so shrunken as to avoid detection at all and that this shrinkage occurred in a rather stepwise fashion. There are also reports in the literature of recordings made from cells much smaller than those normally found in the LGNd of the adult cat using electrodes similar to the ones used in this experiment (Stone & Fabian, 1966). In order for X-cells to be totally functional and only escape detection because of shrinkage, it would seem that this shrinkage must be quite

extreme. It is difficult to imagine that cells could undergo such shrinkage and remain totally functional with all of their receptive field properties intact.

The third, and final, possible explanation to be considered for the results of this experiment is that the former X-cells, after chronic monocular paralysis, respond to visual stimuli as though they were Y-cells. This possibility has far-reaching implications for currently-held models of nervous system function and the presumed correlation of structure and function. Despite the exciting possibilities for this type of explanation, there is little evidence to suggest that such a change can occur in the nervous system. A study of the distribution of conduction velocities from the optic chiasm to relay cells in the LGNd after chronic monocular paralysis would give information concerning this possibility. Without this information, however, interpretation of the results of this experiment in these terms appears far too speculative.

Of these three possible explanations, then, it would appear that the most plausible is that the X-cells in the LGNd are silent and nonfunctional. This is the position which will be adopted in the following discussion of theoretical issues.

Implications of Results for Theoretical Issues

The validity of the X/Y distinction. The essential finding of this experiment, the loss of a specific cell

type from the LGNd of adult cats following chronic monocular paralysis, has been phrased in terms of the X/Y distinction commonly found in the physiological literature. The central issue, however, that of plasticity in the adult cat visual system, does not necessarily rest on the validity of this distinction. In purely operational terms a reduction in the percentage of cells which respond in certain specified ways to certain stimuli has been demonstrated following chronic monocular paralysis. Cells which produce these types of response patterns correspond to cells which are commonly referred to in the literature as "X-cells." In this experiment, likewise, it has been convenient to refer to cells recorded in the LGNd as X-cells or Y-cells. The essential finding of plasticity in the adult visual system is unaltered, however, whether one chooses to categorize cells in this or some other manner.

Despite this relative independence of the experimental result on the validity of the X/Y distinction, the finding has importance for this distinction at several levels. The first of these is a purely empirical one. During the course of the experiment, raw data were quantified descriptively and analyzed to see if it was adequately characterized by two discrete categories. Although several other classification schemes were applied, no other classification scheme appeared to better characterize the

data. Except for a very small percentage of cells (described as "ambiguous" in the results section) all cells appeared to be adequately described by classification as X- or Y-cells. This finding supports previous research designed to delineate or expand this classification scheme.

The results of this experiment also reflect on the validity of the X/Y distinction at a theoretical level. Kaplan (1964) has stated that groupings may be either advantageous or disadvantageous depending on whether they tend to obscure phenomena or allow the discovery of more resemblances than those originally recognized. The discovery of additional resemblances within a group, then, defines the existence of a natural grouping. Much of the current research appears to suggest that X- and Y-cells comprise two natural groups. The original distinction (linearity vs. nonlinearity of summation across the receptive field) has been followed by the discovery of many other distinguishing characteristics. These include differences in responses to many types of visual stimuli, differences in conduction velocity and pharmacological differences. The discovery of these additional differences between groups contributes to the validity of the X/Y distinction.

Likewise, the discovery that it is possible to disrupt one class of cells while leaving the other apparently unaffected contributes to the validity of the distinction.

This experiment, then, in which it was shown that chronic monocular paralysis produces a selective loss of X-cells in the LGNd may be interpreted as giving additional validity to the X/Y distinction.

Implications of this experiment for models of information processing in the geniculostriate system. There are, at present, two opposing models for processing in the visual system. The first of these, the serial processing or hierarchical model (Hubel & Wiesel, 1962;1965a,b), states that processing of visual information is done serially. All axons of cells in the lateral geniculate synapse on the simple cells of visual cortex. The simple cells, in turn, synapse on complex cells. Alternatively, the parallel processing model of connectivity within the visual system (Stone, 1972) states that visual information is conveyed from retina to LGNd and finally to visual cortex by two parallel pathways, one containing X-cells and the other Y-cells. The axons of X-type retinal ganglion cells contact X-cells in the LGNd which then contact primarily simple cells in the visual cortex. The Y-cells in the lateral geniculate receive input from Y-cells in the retina and contact complex cells directly.

Taken alone, the results of Fiorentini and Maffei (1974) raise a problem for the hierarchical model at the cortical level. They report a loss of binocularity which is limited to the simple cell population of the visual

cortex following chronic monocular paralysis. Since, according to the hierarchical model, complex cells are driven by simple cells, it is difficult to see how simple cells could loose binocularity while the complex cells do not. Their experiment, however, does not address the problem of processing between the LGNd and visual cortex.

The results of Fiorentini and Maffei, together with the results of the present experiment, bear on this problem of connection between LGNd and visual cortex. The joint result of these experiments is predicted only by the parallel processing model. Since monocular paralysis has its effect selectively on the simple cell population of visual cortex, any effect which is seen in the geniculate should be limited to the X-cell population. This is exactly the result obtained in the present experiment. Chronic monocular paralysis simultaneously disrupts binocularity among simple cells in the visual cortex and produces loss of X-cells in the LGNd, while at the same time leaving unaffected complex cells in the visual cortex and Y-cells in the LGNd. The results of this experiment, then, taken together with those of Fiorentini and Maffei (1974), are consistent with the parallel processing model.

At the same time, however, these results raise a possible problem for the parallel processing model. According to Fiorentini and Maffei (1974), a certain

proportion of simple cells continue to be driven by the paralyzed eye after monocular paralysis. It is not possible to tell from their report, however, how many this may be. There are two ways in which their effect might have been achieved. One is that the formerly binocular simple cells became nonfunctional leaving as functional only simple cells that were originally monocular. In this analysis, the number of simple cells left in the visual cortex would be greatly reduced by monocular paralysis and it is possible that they were driven exclusively by the remaining X-cell population of the LGNd. This explanation is, of course, the one which is consistent with the parallel processing model. It is also possible, however, that the monocular simple cells reported by Fiorentini and Maffei were binocular before the paralysis but that the input from one eye was suppressed. In this case, the number of simple cells remaining in visual cortex would have been quite large. Such a result would suggest that simple cells do not receive their input exclusively from LGNd X-cells since after monocular paralysis the present experiment found few X-cells responsive to stimulation via the paralyzed eye. This finding may indicate that simple cells do not receive their input exclusively from LGNd X-cells. Thus after monocular paralysis, many simple cells in the visual cortex may be driven by Y-cells in the LGNd. Without knowledge of the fate of the simple cells in the visual cortex, it is impossible to choose between

these two alternatives. Perhaps an answer will be obtained when the ratio of simple cells to complex cells in the visual cortex before and after chronic monocular paralysis is compared.

Locus of Origin for the Physiological Effect of Monocular Paralysis on the LGNd

There are three possible sources for the origin of the X-cell loss in the LGNd of adult cats reported here. The effect could be entirely intraocular. That is, the effect of monocular paralysis could be exerted on the X-cell population of retina and is detectable only in the LGNd because of the loss of synaptic inputs to X-cells there. It is also possible that the effect originates within the geniculate itself and is then transmitted to cortex secondarily. Finally, it is possible that the effect originates in cortex and is transmitted to the LGNd by a retrograde mechanism or through the cortico-geniculate pathway. At this time, of course it is not possible to comment definitively on any of these three alternatives. The data, however, do suggest certain possibilities.

There are several lines of argument which would suggest that an intraocular effect alone cannot explain the effects of chronic monocular paralysis. First, Fiorentini and Maffei (1974) report that the effect on simple cortical cells is symmetrical. That is, after chronic

monocular paralysis an equal number of simple cortical cells continue to be driven by the paralyzed and non-paralyzed eyes. If the effect of monocular paralysis were exclusively intraocular, it would be expected that the cortical effect would be highly asymmetrical with the nonparalyzed driving a far larger number of simple cortical cells. Furthermore, after the completion of this experiment, recordings were made from the layers of the LGNd driven by the nonparalyzed eye in one cat. These subsequent results suggest that, at least after an extended period of monocular paralysis, the X-cell loss in the geniculate may be symmetrical. If this result is replicable in other animals, it also argues against an exclusively intraocular effect. Finally, it may be possible to use the results of monocular deprivation experiments in kittens as an analogue to monocular paralysis.

There are several lines of evidence which suggest that the physiological effects of monocular deprivation in kittens require interocular interaction. First, the retina of monocularly deprived kittens has been examined physiologically and the X- and Y-cell ratios found to be normal (Sherman & Stone, 1973). Secondly, it has been found that binocular competition is necessary to produce the behavioral, physiological and morphological effects of monocular deprivation (Guillery & Stelzner, 1970; Guillery, 1972; Sherman, Guillery, Kaas, & Sanderson, 1974). For

reasons discussed later it may or may not be possible to draw analogies between monocular deprivation in kittens and monocular paralysis in adults. To the extent one can, however, the results of these experiments concerning monocular deprivation would argue that a simple intraocular mechanism cannot produce the types of plastic changes observed in this experiment.

The necessity of interocular interaction does not eliminate the lateral geniculate as a source of the effect of monocular paralysis. Although input from the two eyes does not converge on a single relay cell in the lateral geniculate, cells in adjacent geniculate laminae receive input from homonymous retinal areas and send their axons to a single cortical locus. Interactions between adjacent laminae have been demonstrated both electrophysiologically (Suzuki & Kato, 1966; Lindsley, Chow, & Gollender, 1967; Singer, 1970) and morphologically (Guillery, 1966). It is possible then that the chronic state of incompatible input between the two eyes causes the X-cells to become nonfunctional.

It is also possible that the effect seen in geniculate is mediated by cortex and the interocular interaction which occurs there. There is certainly interocular interaction at this level since input from the two eyes synapses on most cortical cells. The effect could be transmitted to either by a retrograde mechanism or by the corticogeniculate

pathway (Guillery, 1966, 1967). Either of these mechanisms could affect the entire binocular segment of the LGNd and all laminae.

The time course data taken in this experiment, in relation to that for cortex, suggest certain possibilities which deserve mention. Fiorentini and Maffei (1974) report that the loss in binocularity in simple cortical cells occurs rather abruptly, about the seventh or eighth day after monocular paralysis. It is not reported, however, how many cats were sampled during this critical period or how long after the shift they continued to record from cats. Assuming that the results of Fiorentini and Maffei (1974) are an accurate and complete description of the cortical effect, then quite a different picture is obtained in the geniculate. There are two points of loss, one occurring before and one after the cortical effect. This might suggest a dual mechanism for the X-cell loss in the geniculate.

The portion of the X-cell loss in geniculate which occurs after the cortical effect seems most readily interpretable as an effect mediated by, and produced secondarily to, the cortical effect. This is true for a number of reasons. First, from a purely logical standpoint it seems necessary that cause precede effect. Secondly, since the striate cortex receives its primary afferent

input from the lateral geniculate, it is difficult to see how a functional loss of cells in the geniculate could not be reflected in the receptive field properties of cortical cells. The only way this seems possible is if the target cortical calls are already nonfunctional at the time of their deafferentation. Finally, hypothesizing this type of mechanism may help account for some of the individual variability seen in the time course data at the LGNd.

The portion of the geniculate loss which occurs before the cortical loss, however, is somewhat more problematic. Again, it is difficult to see how a functional loss of cells in geniculate could not be reflected in receptive field properties of cortical cells. There seems to be one way, however, in which this is possible. Fiorentini and Maffei (1974) sampled a very small number of cortical cells during the first week after monocular paralysis (20 simple and 17 complex). These cells were dichotomized only as monocular and binocular. There are two ways in which the simple cell population of cortex could become monocular. One is that all of the X-cell inputs to a given cell become nonfunctional at one time. In this case the cell would show an abrupt transition from its formerly binocular state to its new state. It is also possible, however, that the inputs to a target cortical cell from different LGNd X-cells became nonfunctional at different times. In this case the cortical cell would show a very gradual transition

either in ocular dominance or responsiveness. If this were the case then changes in cortical cells might not be detected without recording from a very large number of cells and very careful quantification. This early portion of the geniculate loss, then might be initiated in the LGNd itself, rather than cortex. As has been suggested for monocular deprivation in kittens (Guillery, 1972), these two mechanisms may be very closely related and comprise a reciprocal feedback loop.

The Issue of Adult Plasticity

It seems widely accepted that the adult nervous system is subject to certain types of modification through environmental influences. Certainly, adult organisms are capable of the changes in behavior which are commonly called learning. These behavioral changes are commonly assumed to have neural correlates. Recovery of function after damage to the adult central nervous system is also widely documented in the literature (Meyer, 1974).

The type of plastic change reported in this experiment, however, is of quite a different nature than those commonly assumed to occur in the adult nervous system. In the first place, it occurs in a primary sensory pathway. Secondly, it involves a loss of cells or cell properties, rather than a change or increase in properties. As discussed earlier, plasticity of this nature in mammals had been

observed only in immature nervous system. Both the adaptive value and the morphological bases of this visual system plasticity in immature nervous systems were explained in relation to age-limited factors. This current finding of plasticity in the adult visual system, therefore, may have profound implications for currently accepted explanations of the neural plasticity observed during development.

Before addressing these issues, however, there is another which must be discussed. It concerns the fundamental similarities and differences between the types of plasticity seen in adult and kitten visual system.

The relationship of adult plasticity to kitten plasticity in the visual system. In attempting to compare the nature of the neural changes produced by environmental influences in kittens and adults, two problems arise. One is that none of the manipulations performed on kittens has exactly the same effects on visual experience as does chronic monocular paralysis. The other is that none of the manipulations performed on kittens has exactly the same physiological effects as chronic monocular paralysis. It is not possible to say with certainty, therefore, whether differences in effects are age-related or experience-related.

There are three types of experiments which have been shown to produce plastic changes in kitten visual system. These are experience in a restricted visual environment,

monocular or binocular deprivation of light and pattern vision, and interruption of normal binocular vision without deprivation. Of these three types of experiments, however, little analogy appears between the effects of restricted visual environments and those of chronic monocular paralysis in the adult. Both other types, however, appear to have several features in common with chronic monocular paralysis.

Of experiments which interrupt normal binocular vision without light or form deprivation, the closest parallel to chronic monocular paralysis in terms of its effects on the visual experience is artificial squint. Artificial squint, however, has far less severe consequences on the visual experience of the subject than the monocular paralysis preparation. In the artificial squint experiment (Hubel & Wiesel, 1965a), the medial rectus muscle in young kittens was severed. This produced a large divergence of the visual axes. Other aspects of normal vision were otherwise unaffected. After monocular paralysis not only is there divergent input from the two eyes as in artificial squint but in addition the retinal image in the affected eye is degraded because of paralysis of its intrinsic muscles. The physiological consequences of these two manipulations are similar in one respect. At the cortical level, both manipulations produce a symmetrical loss of binocularity. Chronic monocular paralysis in the adult, however, produces a selective loss of binocularity only in

simple cells while in artificial squint the loss apparently affects both simple and complex cells. It would be interesting to compare the effects of the two preparations at the LGNd. The effects of artificial squint in kittens on the physiology of the lateral geniculate, however, has not been studied.

One analogy which has frequently been alluded to in the course of this discussion is that between chronic monocular paralysis in the adult and monocular deprivation in the kitten. These analogies arise possibly because monocular deprivation has been the most thoroughly studied and consequently the best understood of the manipulations performed on the immature visual system. At the cortical level these manipulations are similar only in that they produce a disruption of binocularity. Monocular deprivation in kittens produces a highly asymmetrical effect, with cells being driven almost exclusively by the nondeprived eye (Wiesel & Hubel, 1963a). This obviously is quite different from the symmetrical loss of binocularity produced by chronic monocular paralysis which is, in this respect, more similar to the loss produced by artificial squint. At the level of the lateral geniculate, however, both monocular deprivation and monocular paralysis have in common the ability to produce a selective loss of a single class of cells. Monocular deprivation in kittens produces

a selective loss of Y-cells, while chronic monocular paralysis in adults produces a selective loss of X-cells.

Both at the cortical and geniculate levels, then, chronic monocular paralysis in adults produces the same types of effects as several of the manipulations performed on kittens. As mentioned previously, however, none of these manipulations is known to have exactly the same effects or combinations of effects. At present it is not known if these differences are related to differences in the preparations or to differences in the age of onset of the manipulations. The answer to this issue could be obtained by recording from adult cats monocularly paralyzed as kittens and adult cats monocularly deprived or rendered strabismic as adults. There are, of course, many possible combinations of outcomes to these experiments which could reveal a great deal about the age-related limits of plasticity in the visual system as well as the mechanisms responsible for the changes reported.

This conclusion, that similar though not identical types of changes are seen in the kitten and adult visual system after environmental manipulation, has been based exclusively on electrophysiological evidence. Microelectrode studies, however, can only reveal the receptive field properties of cells. This conclusion, therefore, is not meant to imply that the morphological bases of the effects reported in kittens and adults are the same. It is possible that very different mechanisms could produce effects which

appear similar at a physiological level. The next section, therefore, will deal in more depth with possible morphological mechanisms which could produce the plastic effects reported after chronic monocular paralysis. Before leaving the issue of adult vs. kitten plasticity, however, it is still necessary to discuss the apparent relative susceptibility of each to environmental influence.

Within the current literature there are two ways in which the relative susceptibility of kitten and adult visual system may be assessed. One is by an examination of the persistence of the effect after normal visual experience is restored. The other is by an examination of the range of ages over which manipulations produce physiological effects.

There is a great deal of literature dealing with the permanence of effects produced in immature nervous systems, particularly with respect to monocular deprivation. In general, the evidence shows that the effects of the early experience are quite permanent and irreversible. Cynader, Berman and Hein (1974) have studied the cortex of adult cats who were visually deprived as kittens but whose deprived eye was opened after the critical period. Although they found some cells which were binocular, recovery was not nearly complete. Much the same situation occurs even if the deprived eye is opened sometime during the critical period (Olsen & Freeman, 1975). The effects

of early visual experience seem to persist, therefore, even if normal visual experience is restored.

There has been little research concerning the range of ages over which most manipulations are effective. Most experiments have initiated the manipulation before the onset of the critical period. There is considerable evidence to suggest, however, that monocular deprivation becomes increasingly ineffective in producing an effect with advancing age (Hubel & Wiesel, 1970; Movshon & Blakemore, 1975). This would seem to suggest, then, that the visual system becomes less plastic with advancing age.

At present it is not possible to make any statements concerning the permanence of the effects of chronic monocular paralysis. The effects of chronic monocular paralysis appear to be permanent for the duration of the paralysis, which when performed by transection of cranial nerves III, IV, and VI is irreversible. There is no currently developed reversible monocular paralysis procedure, however, so the effects of restoring normal vision after a chronic monocular paralysis remain unstudied. The results of such a reversible paralysis on the visual system of the adult cat would be quite interesting.

The issues discussed in this section, then, seem to lead to the conclusion that the adult visual system can show plastic changes very similar to those seen in the

immature visual system. The adult visual system, however, seems to be less susceptible to modification than the immature.

Morphological bases of plasticity in the adult visual system. In addition to the physiological mechanisms which may account for the effects of chronic monocular paralysis it is desirable to examine the possible morphological bases of the effect. The effects of chronic monocular paralysis, at the level of the lateral geniculate must be explained in terms of one of two types of mechanisms. These are cell death, or repression of synaptic transmission without cell death. Cell death, if it occurs, may be either at the level of the LGNd or in the afferent pathway to the LGNd. This mechanism, obviously, implies that the effects of chronic monocular paralysis would be irreversible, regardless of any restoration of normal visual experience or experimental manipulation. Repression, however, implies that connections have not been destroyed and may be demonstrated by the appropriate experimental manipulations.

Since the physiological effects of chronic monocular paralysis are so newly reported in the literature, there have been no investigations of its morphological consequences. It may be, however, that some previously invoked explanatory mechanism for plasticity may appear to account for the data very well. There are two morphological models which could, conceivably, account for the effects of monocular paralysis in the adult cat. These are mechanisms

used to explain plasticity in the immature visual system, and mechanisms used to account for other types of plasticity in adult nervous systems.

The mechanism most commonly invoked to explain developmental plasticity in the visual system is synaptic in nature and generally referred to as functional validation. That is, during neural development, activity of a very specific nature is required for the normal maturation and survival of synapses. If this activity does not occur, then synapses will become ineffective in driving the postsynaptic element and subsequently degenerate. Two aspects of functional validation seem to be critical in explaining developmental plasticity in the visual system. First, functional validation acts to select which synapses will actually remain or become functional among those formed at an earlier period. Secondly, adequate stimulation appears to be required only for a short period during the developmental sequence of the organism. Once a pathway has been functionally validated, further activity is not required for the maintenance of the validated synapses.

Wiesel and Hubel (1963a) extend this concept to include the notion of competition. In the competition model synapses actively compete with each other for space on postsynaptic elements. Activity at a certain set of synapses gives them an advantage in this competition and the ability to suppress the effects of all synapses.

Consequently, those synapses at which appropriate activity occurs come to dominate the activity of the post synaptic cell, while all other synapses become ineffective in exciting the cell and may disappear. At the end of the critical period, then, synapses which have survived competition become functionally validated and establish permanent control over the post synaptic cell. Using the mechanism of functional validation, it is easy to see how the effects of many experiments in kitten visual system may be explained.

In the adult nervous system the mechanism of functional validation has been used to account for learning and memory (Hebb, 1949; Milner, 1957). The only modification which is needed is to hypothesize that simultaneous activity in appropriate loci is the specific activity which is required.

Functional validation cannot, however, be used to explain the plasticity in the adult nervous system following chronic monocular paralysis. During development and the critical period, the subjects of this experiment were not exposed to any manipulations of the visual environment. Presumably, then, they experienced a normal visual environment, and synapses in their visual systems were functionally validated in the normal manner. Once a system has been functionally validated in a specific manner, its properties are fixed. Functional validation, therefore, cannot explain the loss of cells or cell properties in a nervous system

where they previously existed after the termination of the critical period.

A second plastic mechanism, collateral sprouting, has been described in adult and immature nervous systems and is frequently invoked to account for recovery of function after lesions (Goodman & Horel, 1967; Moore, Bjorklund, & Stenevi, 1971; Raisman, 1969; Goldman, 1974). After an electrolytic lesion in a nucleus of the central nervous system, the remaining afferent axons grow new collaterals or "sprout." Furthermore, Moore, Bjorklund and Stenevi (1971) have demonstrated histochemically that after sprouting in an adrenergic system there was an increase in the amount of norepinephrine and in the number of adrenergic terminals correlated with the sprout growth. These results are strong evidence to suggest that these collateral sprouts become functional in forming synapses and transmitting neural impulses.

The phenomenon of collateral sprouting could, conceivably, be used to explain the effects of chronic monocular paralysis at the LGNd or cortical levels. In order to do this, however, one must hypothesize cell death at either the retinal or geniculate level. If such death occurred, then the remaining cells would simply sprout new collaterals which would fill the synaptic space vacated by the dead cells. The target cells, then, may show new properties because of their changed afferent inputs.

Collateral sprouting, obviously, has a great deal of appeal for explaining recovery of function after damage to the central nervous system. It is essentially the first report of morphological plasticity in the adult mammalian nervous system. It has, however, several limitations which suggest that it cannot account for all recovery phenomena (discussed in detail by Geschwind, 1974).

There are also several reasons why it appears unlikely that collateral sprouting could account for the effects of chronic monocular paralysis. First, collateral sprouting has been reported only following direct central nervous system damage such as electrolytic lesion. There is no evidence that sprouting can occur in response to environmental stimulation or in an undamaged nervous system. Caution must be used, therefore, until this possibility is explored empirically. Perhaps the most serious objection, however, is the time course reported for sprout growth. Moore, Bjorklund, and Stenevi (1971) report that some effects were seen as early as 5-15 days. The effect was not marked, however, until 30-60 days. Raisman (1969) reports a time course of 6 weeks. This, obviously, is far longer than the period reported critical for the effects of chronic monocular paralysis at either the cortical or lateral geniculate level.

One mechanism which has frequently been used to explain plasticity in the nervous system is that of synaptic

repression without ultrastructural or functional alteration. Only recently, however, has this phenomenon been demonstrated. Scott (1975) reported that foreign synapses on extraocular goldfish muscle can remain present and physiologically functional, but were repressed after reinervation by the original nerve. Similar phenomena have also been reported in mammalian muscle (Frank, Lømo, Nicolaysen, & Westgaard, 1973; Frank, Jansen, Lømo, & Westgaard, 1974). In these experiments the repression occurs quite rapidly, within a few days of reinervation.

Obviously this type of demonstration on pheripheral nerve-muscle junction is far removed from the effects of chronic monocular paralysis in the central nervous system. This type of explanation, however, does have certain appeal for explaining the effects of chronic monocular paralysis. Recent work by Kratz and Spear (1975) has suggested that repression of synapses, rather than any functional alteration, is responsible for the cortical effects of monocular deprivation. In this experiment Kratz and Spear monocularly deprived kittens during the entire critical period. The nondeprived eye was then enucleated after the critical period. Following enucleation, there was an increase in the proportion of cells which could be driven by the deprived eye, even though this eye remained closed. Furthermore, this shift occurred within a day of the enucleation.

It is possible that synaptic repression after chronic monocular paralysis might be demonstrated experimentally in a number of ways. It is necessary to demonstrate that after chronic monocular paralysis the physiological effects could be reversed quite quickly by some experimental manipulation. Monocular paralysis, performed in such a way that it is reversible, or enucleation experiments analogous to those performed by Kratz and Spear (1975), may prove effective. Any manipulation which does not produce a reversal, of course, does not mean that synaptic repression does not occur. This simply indicates that repression has not been demonstrated.

Adaptive value of adult plasticity. In a preceding section it was shown that the types of plastic changes, at least as could be detected by electrophysiological studies seen after chronic monocular paralysis in the adult, were of a very similar nature to those seen in kitten visual system. It was concluded, however, that there appears to be less plasticity in the adult visual system than in the immature visual system. This conclusion raises questions of an evolutionary nature. Is plasticity in adulthood adaptive in the same ways as it is during infancy? If adult plasticity is adaptive, then why is some plasticity lost after maturation? There are, of course, no definite answers to these questions. Speculation, however, raises many intriguing possibilities.

It is commonly accepted that plasticity in the immature organism is adaptive, both for the individual and for the species. At least one theorist (Schmalhausen, 1949) views developmental plasticity as critical to the adaptation of a species to a new and extreme environment. During the developmental period of an individual, exposure to an extreme environment can produce variation of phenotype which is more adaptive in the extreme environment than the phenotype normally expressed. This type of change requires no genotypic alteration and allows a species to survive in a new ecological niche before genetic modification of the population can occur. Should this extreme environment prove to be permanent, genetic mutations, which are better adapted, may arise and accumulate to form a new species. This process, the Baldwin effect, is considered by many to be fundamental in vertebrate evolution.

It is easy to see then, how the results of the experiments on plasticity in the kitten visual system may be interpreted in these terms. The visual system modifications reported are presumably phenotypic in nature and have obvious survival value. They fit very nicely with Schmalhausen's views of the function of the developmental period.

This view, however, of the adaptive nature of developmental plasticity in the visual system was based on the assumption plastic changes were not possible in adulthood. Consequently, the morphogenetic developmental period was

assigned a very special role in the adaptive process. Since it has been demonstrated that plasticity does occur in the adult visual system, it is necessary to question its role, if any, in the adaptive process.

It would seem that plasticity in the adult could be quite advantageous in a number of ways. First, adult plasticity could be quite important to the survival of individuals within a population. The possibility exists that an extreme environment could arise which proved to be quite transient. Individuals born at a time such that their developmental sequence, and consequently phenotype, was altered by this environment would be favored during its duration. If the extreme environment proved to be transient, however, those individuals with altered phenotypes may be in a very poor state of adaptation in the normal environment. Such is the case with monocularly deprived kittens. If the deprived eye is opened after the critical period, the animals are found to be behaviorally blind in the formerly deprived eye (Wiesel & Hubel, 1963a). Although some behavioral recovery has been reported, this recovery requires very extensive training to which there is no analogue in the natural environment and is not nearly complete (Ganz & Fitch, 1968; Dews & Wiesel, 1970). Within a natural environment, then, these animals would be at a severe disadvantage. Plasticity in adulthood, however,

would allow the individual to readjust to a normal environment should it be restored during his lifetime.

Secondly, adult plasticity could be quite important to the survival of the species. At any given time a very small portion of a population is in infancy. At the onset of the extreme environmental conditions, then, only a few members of the species are capable of having their developmental sequence altered. If the adult members of the species are so poorly adapted in the extreme environment that their survival is threatened, a sharp drop in population numbers could occur. In order to insure large numbers of a phenotypically altered population, then, adult members of the species must survive, at least long enough to replace themselves reproductively. In general, the more members of the population which can undergo phenotypic modification, the smoother the transition from one niche to another.

These views are not necessarily antithetical to commonly accepted evolutionary theory. The Baldwin effect does not require alteration of the developmental sequence, only that phenotypic variation occur in members of a species. Developmental plasticity is only one mechanism by which phenotypic adaptation to a new niche can occur.

Given that adult plasticity could be adaptive, then, the next question which arises concerns the relative extent of adult and developmental plasticity. Since adult

plasticity is potentially adaptive, why should there be a decrease after infancy? On the surface it would seem that the greater the plasticity within a species the greater its chances of survival regardless of extreme environmental conditions. This argument is frequently used to explain the relative success of mammalian species over other, less plastic groups.

Although plasticity is generally adaptive, the situation may arise in which too much plasticity is maladaptive. Under normal circumstances it is desirable that a population conform to a norm and not be subject to morphogenetic fluctuations produced by slight or transient variations in environmental conditions. Phenotypic variation in response to very slight alterations in the environment means that the population is in a constant state of flux. Schmalhausen (1949) expresses this view with respect to developmental plasticity. The normal phenotype which is expressed by a given phenotype is very robust. It is produced by a wide variety of environmental conditions. Only when environmental conditions vary beyond critical limits is the phenotype altered.

This same argument seems to be even more true of adult plasticity. In all species adulthood is of much greater duration than immaturity. This means that during adulthood there is a much greater probability that an organism will be exposed to any number of extreme but

highly transient environments. If phenotypic alteration of a relative permanent nature results from all of these, then the organism could, potentially, spend a major portion of its adult life maladapted in the normal environment.

As pointed out earlier, extreme, but transient, environmental conditions can alter the development of only a very few members of a species (that is, those in infancy because adults are less plastic). Although this alteration would be maladaptive for these few individuals, it is not critical to the survival of the species since they represent a small and easily replaceable portion of the population. If an entire population is altered by a transient environment, however, and return to the normal phenotype takes time, then there is an extended period in which all of the members of the species are poorly adapted. Adulthood, then, should be viewed as a stabilizing factor within a population and a safeguard against the effects of transient environmental conditions. Adult plasticity can be seen as adaptive only in highly specialized situations such as if it readapts the organism to the population norm, occurs only in response to necessarily permanent conditions (such as injury) or is quite transient such as the effect reported by Creutzfeldt and Heggelund (1975).

Adaptive value of the physiological effects of chronic monocular paralysis. In the preceding section the adaptive

value of adult plasticity, in general, was discussed. It is now possible to ask the question: "Is there any adaptive value to the physiological effects of chronic monocular paralysis?" On the surface it might appear that there is never any adaptive value in losing an entire class of cells or cell properties. This might not be the case, however. Monocular paralysis produces incompatibility between the inputs from the two eyes in several ways. This situation should be quite distressing to the subject and greatly alter his perceptions. Perhaps by shutting down inputs selectively he is able to make more efficient use of the remaining ones.

This point is illustrated by the experiment in which kittens were reared with artificial squint. Following surgical misalignment of the visual axes by cutting the medial rectus, most cells in the visual cortex were found to be monocular. On the surface this result may appear to be maladaptive. The kittens have lost the ability to fuse binocular inputs and hence to make binocular depth judgments. They had, however, already lost this ability, due to the surgical misalignment. The loss of binocularity, therefore, gives the kitten no increased visual impairment. What the kitten gained was the ability to process visual information from one eye without incompatible impulses from the other eye to interfere with this processing. Behaviorally, this was how kittens were observed to respond.

They fixated with one eye or the other alternately and seemed to have no visual impairment in either eye (Hubel & Wiesel, 1965a).

In the case of monocular paralysis, however, the adaptiveness of the neural response appears far more obscure. The animal is faced with incompatible inputs from the two eyes as is the case with artificial squint. The advantage of maintaining binocularity in complex cells in this situation but not in artificial squint is unclear. The results at the lateral geniculate seem even more difficult to interpret. A third problem concerns the relationship between the inputs from the two eyes. In artificial squint the inputs of the two eyes were constantly related and both eyes were well focused. In this sense it makes no difference to the animal which eye he uses. In monocular paralysis, however, the relationship between the inputs is variable, depending on the position of the mobile eye. There is also no relationship in the immobile eye between the motor command for eye movements and a shift in the retinal image. In addition to all these problems the retinal image from the immobile eye is severely degraded. It might appear, then, that there would be an advantage to the animal in suppressing all inputs from the immobile eye. This is not the situation, however, and the experimental findings must be interpreted as they occur.

Inferences concerning the possible adaptive value of the effects of chronic monocular paralysis can only be based on two types of information: the receptive field properties of various cell types and inferences of the possible roles each class may play in determining visual perception. Ikeda and Wright (1974, 1972) have proposed that X-cells in the retina and lateral geniculate and simple cells in visual cortex function primarily in visual acuity, while Y-cells and complex cells function primarily as motion detectors. These two functions, obviously, are not mutually exclusive. In order to detect motion, cells must be sensitive to changes in pattern. Consequently, they must be able to detect pattern. Likewise, cells which detect patterns are sensitive to temporal changes in pattern, which is how motion is detected. The receptive field properties of these classes of cells, however, suggest that one class of cells is better suited to one function than is another.

If this functional interpretation of X- and Y-cell receptive field properties is accurate, then cats with chronic monocular paralysis should suffer a loss of some visual acuity, particularly for stationary patterns. Informal behavioral observations suggest that this is, in fact, the case. Furthermore, there is some evidence to suggest that by losing X-cells after chronic monocular paralysis the subject may not be suffering any additional visual impairment beyond that produced by the monocular

paralysis itself. Ikeda and Wright (1972) have found that X-cells are highly sensitive to defocusing of the retinal image. X-cells, then, are probably not being optimally stimulated following chronic monocular paralysis, at least by patterns viewed at close distances. Thus, in losing X-cells the subject is not losing visual information which was not already lost. This interpretation of the results of chronic monocular paralysis suggests that the X-cell loss is produced by the paralysis of the intrinsic eye muscles, rather than the extrinsic eye muscles. This hypothesis is certainly subject to experimental verification. It would be necessary to monocular paralyze a subject, but then focus the paralyzed eye. If defocusing were responsible for the effect, it would be expected that no X-cell loss would occur in this experiment.

Clinical Analogies and Implications for Treatment Procedures

As mentioned previously, this report of the physiological effects of chronic monocular paralysis may have strong implications for the treatment of a number of clinical disorders. Since these results were obtained in adult animals they apply to adult onset disorders. Furthermore, the concern is with disorders which have persistent effects on the vision of the individual after the source of the disorder has been corrected. These effects could take many forms such as amblyopia or a failure to achieve binocular fusion

resulting in diplopia, monocular suppression, or alternating fixation. Most of the known clinical disorders which have these persistent effects are congenital or have a very early onset. There are, however, several types of disorders which are primarily adult in onset and do produce these long term effects. Several seem, at least in part, analogous to chronic monocular paralysis as studied in this experiment.

The most obvious clinical analogue to chronic monocular paralysis is unilateral paralytic strabismus. There is, at present, no report of the effects of complete destruction of cranial nerves III, IV and VI on the visual abilities of the individual. Cases in which this destruction has occurred, either because of injury or tumor, have resulted either in complete eye loss or the death of the individual. There are, however, several types of partial paralyses which are available for study.

Perhaps the most directly analogous type of paralytic strabismus is produced by palsies of cranial nerves III, IV or VI. Such palsies may have a number of causes and are generally reported to be adult in onset. Generally, only one cranial nerve is rendered functionless. Cases have been reported, however, in which two nerves are rendered partially or totally nonfunctional. Treatment for the disorder is usually surgical. If it is possible, the cause of the disorder itself is removed. If not, extrinsic eye muscles are altered so that the eyes are

aligned. In the case of palsey of cranial nerve III, refraction is corrected with spectacle lenses (Crone, 1973).

Another type of paralytic strabismus results from palsies of the extrinsic eye muscles. Again, the disorder may affect only a single muscle or several. As is the case with palsies of cranial nerves III, IV and VI treatment usually consists of alteration of antagonistic muscles so that the eyes are aligned (Crone, 1973).

In both of these types of paralytic strabismus, however, surgical realignment of the eyes does not necessarily produce normal binocular vision. Amblyopia is frequently seen as is diplopia for at least part of the visual world.

Another disorder which frequently results in abnormal binocular vision, particularly amplopia ex anopsia, is anisometropia or unequal refraction in the two eyes. Although this condition is usually congenital it can be produced in adulthood by trauma. Treatment usually consists of applying the optimal refraction to both eyes (Duke-Elder, 1969).

The major contribution that studies of plasticity in the adult visual system such as the one reported here can make to clinical practice at present is to show the importance of prompt treatment. It has been widely assumed that delay of treatment in adult-onset disorders was not harmful to the visual abilities of the patient. Usually corrective surgeries are performed in sequence, and may be carried out over a period of many months or even years. Experimental

results such as this, however, indicate that prompt treatment may be essential for the restoration of normal vision.

Future experimentation may prove even more valuable for clinical treatment. Using the monocular paralysis paradigm, it might prove possible to find a technique of retarding the physiological effects of paralytic strabismus, such as occlusion of one eye. These results, in turn, could be applied to human clinical problems.

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