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THE EFFECTS OF MONOCULAR PARALYSIS AND BINOCULAR EYELID SUTURE ON THE ELECTROPHYSIOLOGY OF LATERAL GENICULATE NUCLEUS OF THE CAT

by

Mark Allan Schwartz

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in Partial Fulfillment
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Doctor of Philosophy

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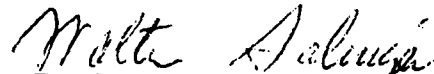
1978

Approved by



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SCHWARTZ, MARK ALLAN. The Effects of Monocular Paralysis and Binocular Eyelid Suture on the Electrophysiology of Lateral Geniculate Nucleus of Adult Cats. (1978)
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Single unit recording of cells in the lateral geniculate nucleus (LGN) of adult cats following monocular paralysis of two weeks duration has been reported to diminish the relative proportion of X-cells in this nucleus. This functional loss of LGN X-cells was detected in the LGN laminae innervated by the paralyzed eye. Limitations in the method of classifying LGN cells as X or Y in the earlier work, however, precluded acquisition of data concerning the proportion of X- and Y-cells in the lamina innervated by the normal eye.

The present study used response latency to optic chiasm shock of LGN cells (OX latency) to divide cells as X or Y. Y-cells have short and X-cells long OX latencies. This measure allows analysis of the effects of monocular paralysis in the layers innervated by the paralyzed and mobile eye, respectively.

Monocular paralysis causes perturbation of the visual system directly related to the failure of the motor system in one eye. These consequences may be divided into those affecting retinally mediated stimuli (pattern and/or binocular vision), or extraretinally mediated stimuli (ocular proprioception and/or corollary discharges). Disruption of either of these two systems could be responsible for initiating the loss of X-cells.

To approach these issues the following questions are asked: (1) Is monocular paralysis followed by a change in the relative proportions of long (X) and short (Y) latency cells in the LGN? (2) Are these changes the same for the LGN layers innervated by the mobile and paralyzed eyes, respectively? (3) Can the loss of long latency cells be attributed to either discordant visual input (retinal mediation) or discordant motoric factors (extraretinal mediation)?

Experiment I compares animals with acute monocular paralysis, eyes open (ACMP; paralysis of four days or less) and chronic monocular paralysis, eyes open (CHMP; paralysis of fourteen or more days). The relative frequency distributions of OX latencies generated by ACMP and CHMP animals for layers A, A_1 and C of the contralateral LGN reveals a functional loss of long latency cells in the CHMP preparation. The effect is, moreover, most pronounced in the layer receiving input from the mobile eye.

The effects of chronic bilateral lid suture on the proportion of X- and Y-cells in the LGN has not been previously determined. The distributions of OX latencies from animals with acute monocular paralysis and chronic bilateral lid suture (ACMP/BISUT), and animals with acute monocular paralysis but permitted normal vision (ACMP), were compared. Results demonstrated the effectiveness of chronic pattern deprivation alone in producing an OX latency distribution shift toward cells with shorter OX latencies only in LGN layer A_1 (Experiment II).

The relative contributions of retinally and extraretinally mediated input to the monocular paralysis effect (Experiment III)are investigated by preventing pattern input during the period of chronic monocular paralysis. A comparison between OX latency distributions recorded in ACMP/BISUT animals, and animals with chronic monocular paralysis and chronic bilateral eyelid suture (CHMP/BISUT) permits assessment of the ability of the nonvisual, proprioceptive effects of monocular paralysis to effect a change in the LGN cell population. Deprivation of pattern input during the chronic paralysis period does not diminish the effects of monocular paralysis on the A&C layers. Consequently, retinal mediation cannot be the basis for the shift of cell latencies observed in Experiment I for the A&C layers. However, monocular paralysis has a detectable effect on the OX latency distributions in the A_1 layer of animals only with concurrent pattern vision and produces no discernable effect on A_1 in the absence of pattern input. Therefore, one can conclude that retinal mediation is required for the distribution shifts produced by monocular paralysis in Experiment I for the A_1 layer.

The pattern of results may be accounted for by a mechanism which is activated by chronic monocular paralysis and is involved in processing binocular interaction in the LGN. This mechanism uses primarily retinally mediated stimuli in processing its impact on A_1, and extraretinal stimuli

(presumably oculomotor) in producing its effects in LGN laminae A&C.

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TABLE OF CONTENTS

LIST OF TABLES

Table | Page

LIST OF FIGURES

CHAPTER I

INTRODUCTION

The visual nervous system can change as a function of experience. That is, it is malleable or plastic. Until recently, however, it has been thought that the physiology of the visual system is subject to modification by environmental factors only during a period restricted to the early weeks of the organism's life (Hubel & Wiesel, 1970). In the kitten, perturbation of visual input alters certain characteristics of neurons only if the perturbation occurs during an early postnatal period. Those same characteristics are unaltered in adult animals subjected to the same conditions. Recent evidence has suggested, however, that the period of plasticity for some neural characteristics extends into adulthood (Buchtel, Berlucci, & Mascetti, 1972; Fiorentini & Maffei, 1974; Brown & Salinger, 1975; Maffei & Fiorentini, 1976). The present study further examines the question of plasticity in the visual system of the adult cat.

Response Characteristics of Cells in the Retino-Geniculo-Striate Pathway of the Normal Cat

Response characteristics of cells in the visual system of the normal cat have recently been the object of extensive research. In visual cortex, for example, the capacity of a unit to be excited by input to either eye (binocularity)

was found to be present in 80% of cells in normal adult cats (Hubel & Wiesel, 1962). The property of cortical cells to respond maximally to linear contours at a particular orientation (orientation selectivity) was also assessed. In cortical Area 17, most cells show orientation selectivity and all orientations are represented in the normal animal (Hubel & Wiesel, 1959, 1962, 1965a).

Examination of response characteristics of 'normal,' visually responsive units outside of cortex have revealed other types of cells. Among them X- (sustained response type) and Y- (transient response type) cells have been found both in the retina (Enroth-Cugell & Robson, 1966; Cleland, Dubin, & Levick, 1971; Fukada, 1971; Cleland & Levick, 1972; Cleland, Levick, & Sanderson, 1973; Cleland, Levick, & Wassle, 1975) and dorsal lateral geniculate (hereafter referred to as the LGN or geniculate) (Cleland, Dubin, & Levick, 1971; Dreher & Sanderson, 1973; Fukada & Saito, 1972; Hoffman, Stone, & Sherman, 1972).

X- and Y-cells have been shown to differ in several properties, including the following: (1) whether they sum the influence of the center and surround regions of their receptive fields linearly or nonlinearly, with X-cells summating linearly and Y-cells nonlinearly (Enroth-Cugell & Robson, 1966), (2) receptive field size with Y-cells having larger surround regions (Fukada, 1971;

Hoffman, Stone, & Sherman, 1972; Cleland, Levick, & Sanderson, 1973), (3) retinal eccentricity with X-cells found predominantly in central retina and Y-cells more frequently found in peripheral retina (Hoffman, Stone, & Sherman, 1972; Cleland, Levick, & Sanderson, 1973; Fukada & Stone, 1974; Ikeda & Wright, 1975), (4) cell size with X-cells having smaller cell bodies (Boycott & Wassle, 1974), and (5) conduction velocity, where X-cell axons conduct more slowly than Y-cell axons (Cleland, Dubin, & Levick, 1971; Fukada, 1971; Fukada & Saito, 1972; Hoffman, Stone, & Sherman, 1972; Fukada, 1973; Cleland & Levick, 1974; Ideka & Wright, 1975; Fukada & Stone, 1976).

Evidence for Neural Plasticity During Early Development

Deviations along several of these dimensions have been observed in immature visual cortex and LGN following environmental manipulations. In these studies, normal visual input is disrupted following exposure to a limited visual environment (e.g., restriction of contours to one orientation, stroboscopic illumination, random dot exposure, unidirectional movement exposure), or following alteration of input to one or both of the kitten's eyes (e.g., lid suture, artificial squint, torsional rotation of the eye).

Among the most striking effects are the modifications in the binocularity of visual cortex cells in kittens following monocular or binocular lid suture.

After only a few days of monocular deprivation during the first three postnatal months, a substantial reduction in binocularity is observed, with the deprived eye unable to drive an appreciable number of cortical cells (Wiesel & Hubel, 1963b; Hubel & Wiesel, 1970; Blakemore & van Sluyters, 1974; Olson & Pettigrew, 1974; Blakemore & van Sluyters, 1975; Movshon, 1976a; Berman & Daw, 1977). Compared to monocular deprivation, binocular deprivation appears to be less damaging to cortical cells. Following binocular lid suture for the first three postnatal months the majority of cortical cells remains responsive to stimulation of either eye (Wiesel & Hubel, 1965a).

Initial attempts to record from cells in the LGN following monocular or binocular deprivation failed to reveal physiological changes comparable to those observed in the cortex (Wiesel & Hubel, 1963a). However, morphological examination of the geniculate does reveal atrophy in the layers innervated by the deprived eyes (Wiesel & Hubel, 1963a; Hubel & Wiesel, 1970). These studies also reported that neither the receptive field properties, nor the morphological changes observed in kittens were found in animals deprived as adults. Subsequently, however, evidence has indicated that changes in geniculate functioning occur in the kitten following both monocular and binocular deprivation. After deprivation during the critical period, the geniculate layers innervated by the

deprived eye show a smaller proportion of Y-cells than in the normal kitten (Sherman, Hoffman, & Stone, 1972; Hoffman & Cynader, 1975).

Normal binocular responsiveness of cortical cells has also been disrupted by surgically induced squint (strabismus) or by alternate covering of the kitten's eyes with opaque occluders (Hubel & Wiesel, 1965b; Blake, Crawford, & Hirsch, 1974). Neither of these procedures appears to substantially deprive the animal of pattern vision. However, there is a defect of pattern input. By misaligning the visual axes, surgically induced squint prevents stimulation of corresponding retinal points by a single contour in the visual field. Alternating occlusion of the eyes also precludes simultaneous binocular stimulation. Both perturbations of binocular input are followed by a decrease in the proportion of cortical cells influenced by both eyes (Hubel & Wiesel, 1965b; Maffei & Bisti, 1976; Yinon, 1976). Mature subjects were not investigated in these studies since previous experiments had shown that monocular or binocular deprivation of adult cats does not result in a loss of cortical binocularity (Wiesel & Hubel, 1963b).

Torsional rotation of one eye has also been used to alter binocular input. Following surgery, the animals are permitted binocular exposure in a normal pattern environment. Eye rotations of 30 to 109 degrees during the first

three months of the kitten's life produces a decrease in the number of visual cortex neurons showing binocularity (Blakemore, van Sluyters, Peck, & Hein, 1975).

Shinkman and Bruce (1977) induced image rotation (16 degrees) in kittens. However, theirs was a nonsurgical procedure wherein the animal is fitted with goggle mounted prisms. Following this type of eye 'rotation' cortical cell recording reveals normal orientation specificity as well as a normal proportion of cells driven by both eyes. However, the preferred direction of the binocular cells differed for stimuli originating in the separate eyes by the degree of rotation experienced during the period of rotation exposure. A similar result was found by Shlaer (1971) who fitted his animals with prisms which introduced a vertical disparity (2-4 prism diopters) between the two eyes. Unit recording in cortex following this insult indicated an abnormal disparity distribution which was shifted in the direction which could compensate for the early exposed disparity.

Kittens have also been reared in a variety of limited visual environments as a means of examining early plasticity. Prolonged exposure in an environment in which linear contours are presented at a single, constant orientation reduces the variety of orientations to which cortical cells respond. The population of cells tends to be biased toward the exposed orientation (Blakemore &

Cooper, 1970; Hirsch & Spinelli, 1970, 1971; Pettigrew, Olson, & Barlow, 1973; Pettigrew, Olson, & Hirsch, 1973; Blakemore, 1974; Pettigrew & Garey, 1974; Peck & Blakemore, 1975). Exposure to a unidirectional environment also appears to alter cortical cells such that a greater than normal proportion of cells are directionally selective for the pre-exposed direction (Tretter, Cynader, & Singer, 1975; Daw & Wyatt, 1976; Berman & Daw, 1977).

Kittens reared without access to linear shapes also appear to have cortical cells that respond preferentially to the previously exposed nonlinear stimuli. That is, rearing with visual experience limited to a pseudorandom array of point sources of light produces a cortex with cells preferring circumscribed bright targets instead of oriented lines (Pettigrew & Freeman, 1973).

Rearing in stroboscopic illumination has also been used to alter response properties of cortical neurons. After stroboscopic rearing, the proportion of cells in visual cortex that are direction selective is substantially reduced when compared to normally reared animals (Cynader, Berman, & Hein, 1973; Olson & Pettigrew, 1974; Cynader & Chernenko, 1976). Further, the number of cells influenced by both eyes is diminished (Olson & Pettigrew, 1974).

Evidence for a Sensitive Period for Neural Plasticity

The possibility of a maturational decline of sensitivity for neural plasticity was first investigated by Wiesel and Hubel (1965b) and Hubel and Wiesel (1970). Since that time, several studies have lent support to the hypothesis that some characteristics of cells in kitten cortex appear susceptible to environmental influence only during a three-month postnatal period.

Monocular deprivation during this early postnatal period produces cortical cells that are responsive only to the exposed eye (altered binocularity). The deprived eye influences a substantially reduced number of cells (Wiesel & Hubel, 1965b; Hubel & Wiesel, 1970; Blakemore & van Sluyters, 1974; Blake & Hirsch, 1975; Movshon, 1976a; Berman & Daw, 1977). Several studies have examined the temporal limits of the sensitive period by attempting to counteract the cortical effects of monocular deprivation. The methods used either involve opening the originally closed eye and suturing the originally open eye (reverse suturing), or permitting the animal normal vision after a period of monocular deprivation. Neither of these procedures, if begun after the first three months of life, is capable of reversing the effects of monocular deprivation.

Reverse suturing, at 4-5 weeks of age, does alter the effects of monocular deprivation. This procedure yields a cortex with cells responsive only to the

originally closed but last open eye (Wiesel & Hubel, 1965b; Blakemore & van Sluyters, 1974; Movshon, 1976a; Berman & Daw, 1977). By 14 weeks of age, reverse suturing is ineffective (Blakemore & van Sluyters, 1974). Attempts to alter the binocularity of cortical cells in adult animals by lid suture have also not been successful (Hubel & Wiesel, 1970). Thus a critical period for binocularity seems to have been demonstrated.

A critical period also exists for determining direction of movement specificity in the neo-natal kitten. Most cortical cells have a preferred direction to which they respond. That is, cells respond maximally to a moving target when the target travels in a given direction. Response rate is decreased from this maximum if the target moves in any other direction. Daw and Wyatt (1976) first raised a series of animals for 3 1/2 to 7 weeks in an environment limited to vertical stripes moving in one direction. At varying times after onset of selective exposure (from 3-7 weeks) the direction of the stripe movement was reversed. This procedure is similar in design to the reverse suturing used to investigate the temporal limits of plasticity of binocularity following monocular deprivation. The data indicate that if reversal of stimulus direction or motion occurs earlier than four weeks, cortical cells respond selectively to the reversed movement direction. If reversal of direction occurs later

than 5 weeks of age, cortical cells continue to manifest selective response to the first exposed stripe direction (Daw & Wyatt, 1976; Berman & Daw, 1977). These results suggest that: (1) cortical cell plasticity for direction of movement ends around 5 weeks of age, and (2) the onset and end of the critical period of plasticity for direction of movement occur earlier than that for binocularity.

Developmental studies have also defined a sensitive period for environmental alteration of orientation specificity. Although there are conflicting reports as to whether neo-natal cortical cells are innately endowed with orientation specificity (Hubel & Wiesel, 1962; Barlow & Pettigrew, 1971; Buisseret & Imbert, 1975), it is generally accepted that recording from cortices of kittens permitted exposure only to a particular orientation yields a predominance of units responsive only to that orientation (Blakemore & Cooper, 1970; Hirsch & Spinelli, 1970, 1971). That is, after neo-natal exposure to either vertical or horizontal bars, cells recorded in cortex are biased such that they respond only to the previously presented stimuli.

Development of some cell properties in LGN also appears to be bound by a critical period. As mentioned, initially little functional effect was observed in LGN following environmental alterations. However, morphological changes were seen. Subsequent to monocular deprivation,

cells in the deprived geniculate layers are smaller (cell area decreased by 40%) when compared to cells in the non-deprived layers (Wiesel & Hubel, 1963a; Kupfer & Palmer, 1974).

Attempts made to reverse the morphological effects of monocular deprivation in the geniculate indicate that, as with cortical cells, geniculate cells are maximally sensitive to modification during the three months after birth. Dursteler, Garey, & Movshon (1976) deprived kittens of vision in one eye until between 5 and 14 weeks of age and reverse sutured for a further 3-63 days. Reversal was most effective in altering geniculate morphology if initiated at the age of 8-14 weeks. Similar results have been reported by Wiesel & Hubel (1965b) who deprived kittens for 3 months and then reverse sutured for 14 additional months. They determined that cells innervated by the initially deprived eye did not grow, but that cells innervated by the second deprived eye did show some atrophy.

In summary, it appears that, at least for the effects of monocular deprivation and some selective exposure perturbations, sensitive periods for physiological and morphological organization do exist during the first months of life.

Evidence for Neural Plasticity Extending Beyond Periods of Early Development

Buchtel, Berlucci, and Mascetti (1972) were the first to study the effects of monocular paralysis on the

adult visual system. Following denervation of the intrinsic and extrinsic ocular muscles they found a decreased proportion of binocular cortical cells. A more recent report using a slightly different technique for eye immobilization supports this result. Fiorentini and Maffei (1974) unilaterally resected the lateral rectus muscle and cranial nerves III and IV. Extracellular recording in visual cortex during the first week after surgery revealed a decreased proportion of binocular simple cells, while the proportion of binocular complex cells remained unchanged.

Because the geniculate is intermediate between retina and visual cortex, changes in binocularity observed in cortex following monocular paralysis might be accompanied by changes in binocularity in geniculate cells as well. However, LGN cells do not receive converging excitatory input from both eyes as do many cells in visual cortex. Rather, direct excitatory input to a geniculate cell is monocular. Cells located in layers A&C receive afferents direct from the contralateral eye and cells in layer A_1 receive axons of ipsilateral retinal ganglion cells (Guillery, 1970; Kaas, Guillery, & Allman, 1972). Since LGN cells are not binocular in the same sense as cortical cells, alteration in degree of binocularity relevant in demonstrating cortical modifications

subsequent to monocular paralysis may not be an appropriate dimension to observe changes in the geniculate.

However, the X- and Y-cell populations in geniculate have been shown previously to be differentially sensitive to environmental manipulations of visual input in kittens (Sherman, Hoffman, & Stone, 1972; Hoffman & Cynader, 1975) paralleling the effects described for binocularity in cortex. Therefore, these two populations serve as reasonable foci for the search in LGN for parallels to the cortical plasticity displayed consequent to monocular paralysis.

Working with X- and Y-cells in the LGN of adult cats, Brown and Salinger (1975) have also reported the selective functional loss of one of these cell types following monocular paralysis. After monocular immobilization of 14 days or more, a significant decrease was found in the proportion of X-cells recorded in the geniculate layers receiving afferents from the immobile eye. Their report, as well as studies of Buchtel, Berlucci, and Mascetti (1972) and Fiorentini and Maffei (1974), supports the use of X- and Y-cell populations to further explore geniculate plasticity beyond what has been termed the critical period.

Purpose of the Present Study

Brown and Salinger (1975) investigated the proportion of X- and Y-cells recorded in LGN after chronic monocular

paralysis. Their study was a preliminary attempt at demonstrating the existence of adult geniculate plasticity and as such was of limited scope. The data depended upon cellular response to visual stimuli in order to classify LGN cells as X or Y. This procedure rests upon a precise and complex mapping of receptive field organization. Classification of cells based upon receptive field analysis, while adequate to expose the selective functional loss of LGN X-cells in the lamina innervated by the paralyzed eye, has technical limitations.

One limitation of receptive field analysis as used in Brown and Salinger (1975) is that it cannot be used to differentiate X- and Y-cells in the geniculate layer innervated by the unoperated, mobile, normal eye. This is true since the monocular paralysis preparation does not immobilize both eyes and receptive fields cannot be mapped for a moving eye.

A second limitation concerns the inadequacy of receptive field analysis to permit the elevation of the alternative explanations for the selective X-cell loss in Brown and Salinger (1975). The selective functional loss of X-cells following chronic monocular paralysis could have resulted either from the selective atrophy of LGN X-cells or from a functional change such that after chronic monocular paralysis LGN X-cells respond to visual stimuli as if they were Y-cells. If LGN X-cells alter their receptive

field characteristics such that they respond as Y-cells, receptive field analysis itself cannot distinguish altered X-cells from Y-cells. This is true since any Y-cells recorded in geniculate may in fact be X-cells whose characteristics now appear to be of the Y variety. In order to determine whether X-cells atrophy or change their receptive field characteristics, a measure is required which is not dependent upon receptive field analysis and which nonetheless continues to discriminate X- from Y-cells after monocular paralysis.

A measure which permits investigation of (1) changes occurring in the LGN layer innervated by the mobile eye, and (2) evaluation of alternative explanations for the results of Brown and Salinger (1975), is that of latency of LGN cell response to optic chiasm shock. The latency of LGN cell response to optic chiasm shock measures the length of time between electrical stimulation of the optic chiasm and the response to this stimulation as recorded extra-cellulary in the ipsilateral LGN. As indicated previously, conduction velocity and therefore latency of response to optic chiasm shock, has been found to adequately differentiate X- and Y-cells in retina (Cleland, Dubin, & Levick, 1971) and geniculate (Cleland, Dubin, & Levick, 1971; Hoffman, Stone, & Sherman, 1972). Hoffman, Stone, and Sherman (1972) report that Y-cells located in the LGN respond to shock applied to the optic

chiasm with a shorter latency than do X-cells. One hundred percent of all Y-cells have latencies to optic chiasm shock of less than 1.9 msec (short latency cells), whereas one hundred percent of all X-cells have latencies greater than 1.5 msec (long latency cells). This relationship between optic chiasm latency and the two cell types makes possible not only observations on the effects of monocular paralysis on X- and Y-cell populations in LGN but also makes possible investigation into the questions raised above which could not be addressed using the receptive field analysis measure of Brown and Salinger (1975).

First, the optic chiasm latency measure does not depend on receptive field analyses for differentiating LGN X- and Y-cells. Therefore, it permits analysis of the effects of monocular paralysis on the geniculate layer innervated by the ipsilateral, normal eye.

And second, the optic chiasm latency measure permits analysis of alternative explanations for the functional loss of LGN X-cells described by Brown and Salinger (1975). The loss of LGN X-cells after chronic monocular paralysis could have resulted either from the selective atrophy or suppression of geniculate X-cells or from a change in the receptive field characteristics of X-cells. If the observed loss of geniculate X-cells were a consequence of geniculate X-cells assuming the receptive

field properties of geniculate Y-cells, then a concomitant change in conduction velocity (and therefore latency) of retinal ganglion X-cells (long latency) towards the retinal ganglion Y-cell range (short latency) would not be expected. This is true since the axons of retinal ganglion cells do not have access to binocular information and thus pre-geniculate effects of monocular paralysis, including changes of axonal conduction velocity, seem unlikely. If, however, the observed loss of X-cells in Brown and Salinger is due to selective atrophy or suppression of LGN cells of the X type, a distribution of LGN cell latencies to optic chiasm stimulation would be deficient in those latencies usually attributable to the X-cell population.

And finally, the optic chiasm latency measure permits investigation of the complex visuomotor disturbances produced by monocular paralysis. Unilateral ocular paralysis causes disturbances of the visual system directly related to the failure of the motor system in one eye. First, visual anomalies including failure of conjugate gaze, pupil asymmetry, and unilateral failure of accommodation, result in discordant visual input. These all entail alteration of the normal retinal input initiated by the paralysis, and are hereafter referred to as 'retinally mediated' effects. Second, concordant, symmetric motoric signals (either feedback from afferent fibers of

extraocular muscles or corollary discharges) normally associated with eye movements are interrupted. These are a class of consequences of eye paralysis that are not concerned with retinal input and are therefore labeled 'extraretinally' mediated effects. Either of these classes of consequences could initiate the possible loss of longer latency (X) cells.

In order to evaluate alternative interpretations of previously described effects of monocular paralysis on the LGN, and to begin to assess the relative contributions of retinally mediated and extraretinally mediated signals in producing these effects, the following questions are asked in the present study: (1) Does monocular paralysis produce a change in the relative proportions of long and short latency cells in the LGN?, (2) Are these changes the same for the geniculate layers innervated by the paralyzed and mobile eyes, respectively?, (3) Can the changes be attributed to either discordant visual input (retinally mediated factors) or discordant motoric input (extraretinally mediated factors)?.

Experiment I examines the first and second questions by comparing the frequency distributions of response latencies to optic chiasm shock for LGN cells (layers A&C and A_1) in control animals and animals with chronic monocular paralysis. In order to estimate the relative

contributions of discordant pattern vision and disrupted motor input to the expected loss of long latency cells, comparison between distributions of LGN cell latencies to optic chiasm shock found in animals with acute monocular paralysis and closure of both eyes (ACMP/BISUT) and animals with chronic monocular paralysis and closure of both eyes (CHMP/BISUT) are made in Experiment III. If changes in optic chiasm latency distributions similar to those in Experiment I are found in geniculates of animals deprived of patterned visual input during the period of chronic paralysis, then discordant visual input (retinally mediated factors) cannot be required for the observed changes.

Since little is known of the effects of adult onset lid suture used in Experiment III on the optic chiasm latency distributions of LGN cells, caution dictated the inclusion of Experiment II. In this study, the effect of bilateral lid suture (fourteen days or more) on the distributions of optic chiasm latencies of geniculate cells is explored by comparing animals with acute monocular paralysis and permitted normal pattern vision for the period prior to recording (ACMP) with animals prepared with acute monocular paralysis but deprived of patterned visual input for two weeks prior to geniculate recording (ACMP/BISUT).

CHAPTER II

METHOD

Subjects

Fifteen adult cats of unknown pedigree were purchased from a local source, maintained on ad lib food and water, and housed according to applicable FDA regulations. Supervision and medical attention as required were provided by a local veterinarian.

All subjects were prepared with left eye immobilization and implanted with cranial bolts. Seven of the fifteen subjects were, in addition, prepared with bilateral eyelid suture always of two weeks duration. Surgical intervention was introduced to four groups of animals at varying times during the course of the experiment. Summary of the duration for monocular paralysis for each group is found in Table 1.

The ACMP animals (acute monocularly paralyzed, eyes open) were permitted pattern vision prior to and after paralysis of the left eye. They were recorded on the day of monocular paralysis surgery and up to three days thereafter. CHMP animals (chronic monocularly paralyzed, eyes open) were also permitted normal pattern vision prior to and after paralysis of the left eye. They were recorded fourteen or more days after monocular paralysis surgery.

Table 1

Summary of the Duration for Monocular Paralysis and Bilateral Eyelid Surgeries

Condition	No. of Ss	Duration Paralysis	Duration Lid Suture
ACMP	4	≤ 4 days	-
CHMP	4	≥14 days	-
ACMP/BISUT	4	≤ 4 days	≥14 days**
CHMP/BISUT	3	≥14 days	≥14 days*

ACMP = acute monocularly paralyzed, eyes open

CHMP = chronic monocularly paralyzed, eyes open

CHMP/BISUT = chronic monocularly paralyzed, eyes closed (bilateral lid suture)

ACMP/BISUT = acute monocularly paralyzed, eyes closed (bilateral lid suture)

*bilateral lid suture on same day as paralysis surgery

**bilateral lid suture 14 days before paralysis surgery

The ACMP/BISUT animals (acute monocularly paralyzed, eyes closed) were bilaterally eyelid sutured fourteen days before onset of left eye paralysis and recording. The CHMP/BISUT animals (chronic monocularly paralyzed, eyes closed) were monocularly paralyzed (left eye) and bilaterally lid sutured at the same time, fourteen days prior to recording.

Surgical Preparations

Eye immobilization. Paralysis of the left eye in each animal was produced by transection of cranial nerves III, IV, and VI at the point of their common entry into the orbit. The cats were anesthetized with intraperitoneal injections of acepromazine maleate and sodium pentobarbital. Vital signs were monitored throughout the procedure, and temperature was regulated with a feedback controlled heating pad. The animal was positioned in a restraint device, in the supine position, allowing visualization of, and access to, the roof of the mouth. The tongue was retracted with an atraumatic retractor and the soft palate incised at a point 1-2 mm posterior to the caudal edge of the palatine bone. The incision extended 3-6 mm in a caudal direction and was expanded laterally using a small retractor. The mucosa of the nasopharynx was located approximately 6 mm deep to the initial incision and was visible through the retracted tissue. This tissue covers the ventral aspects of the

presphenoid bone, the basisphenoid bone, and a transverse suture running between these two processes. The mucosal tissue was removed using a large dental burr, exposing these landmarks. The posterior portions of the presphenoid bone were then removed using the large dental burr. Removal of the presphenoid commenced on the midline just anterior to the transverse suture and proceeded anterior and lateral. Removal of this bone exposed the sphenoid sinus and, more deeply, a bone cover encasing the optic nerve, optic chiasm, and optic tract. Cranial nerves III, IV, V, and VI are encased in a bony, vascularized sheath just lateral to the optic chiasm, running obliquely to the anterior/posterior axis. In order to expose these nerves, while preserving the integrity of the bone covering the chiasm, optic nerve and tract, a small dental burr was used to remove the ventral aspect of the bony sheath just lateral to the optic chiasm. Careful removal of the sheath exposed the vento-medial edge of the vascular bundle (Mandibular rete) encasing the motor nerves innervating the eye. From this point, the bone covering the vascular bundle was removed 1-2 mm in the anterior and posterior direction. Subsequently, the lateral and medial edges of the bone sheath were removed. This procedure completely exposed the vascular bed surrounding the nerves.

Careful dissection of the vascular tissue, using gelfoam, topical epinephrine and aspiration as needed to

control bleeding, exposed cranial nerves III, IV, V and VI. Exposure of the nerve bundle in this fashion permitted visually guided dissection and thus assured the transection of the proper fibers. Careful dissection of the tissue surrounding the nerves permitted isolation of the individual nerve trunks. Cranial nerve III is located just lateral to the medial edge of what remains of the bony sheath that initially covered the nerves and vascular bed. Nerve IV is found lateral and dorsal to nerve III. Nerve V lies just lateral to III and IV, and nerve VI is just lateral and ventral to nerve V. After visually verifying the positions, cranial nerves III, IV and VI were transected individually and in sequence. Care was taken not to disturb cranial nerve V. Hemostasis was achieved using gelfoam and aspiration as needed. Topical antibiotic was applied prior to closing the incision. Once assured of hemostasis, eye immobilization was verified visually. The palate was then closed using 4/0 silk sutures.

It is important to note that the surgery does not invade the cranial cavity since the meninges remain intact. Also, the surgery cannot produce accidental damage of orbital contents or cranial nerve II since their bony coverings are left intact.

Lid suture. Bilateral lid suture was performed on seven animals. The nictitating membrane was sutured to the underside of the upper eyelid in the following manner.

Using forceps, the nictitating membrane was drawn obliquely from its infero-medial position to a supero-lateral position and stitched to points on the upper lid near the lateral canthus of each eye. To protect the nictitating membrane from dessication, the eyelids were also sewn together. Daily inspection of eyes was made to insure continued complete closure.

Cranial pedestal and craniotomies. In order to permit mounting of the animal's head in the stereotaxic plane during recording without the use of painful eye and ear bars, a cranial pedestal was positioned on the first recording day. This procedure is patterned after that of Orem, Schlag-Rey, and Schlag (1973) and involves the implanting of three bolts, heads inverted and inserted into keyhole shaped craniotomies. The head of each bolt is thus interposed between skull and intact dura with the threads extending approximately one-half inch above the skull. Three more bolts are positioned in a stainless steel head holder and positioned next to the implanted bolts. These three pairs of bolts are then embedded in dental acrylic forming a rigid pedestal. This procedure permits preparation of an easily tended animal, held for repeated microelectrode recording in the stereotaxic instrument without the usual painful pressure points from the stereotaxic headholder.

Simultaneous to pedestal preparation, craniotomies were also performed over the right LGN (A 3.0-8.0, L 8.0-12.0) and the right side of the optic chiasm (A 14.5, L 2.0) (Snider & Neimer, 1961).

Apparatus

Recording. Extracellular recording of single units in the LGN was made using stainless steel microelectrodes purchased from Frederich Haer and Company. These electrodes are insulated with Epoxylite, with tip diameters of approximately 1 micron and an impedance of 7-15 megohms at 1000 Hz. Unit activity was amplified by a WPI DAM-5 preamplifier and a Grass AC amplifier. The output was viewed on a Hewlett Packard 141A Storage Oscilloscope and monitored by an audiomonitor. Output was stored on magnetic tape for subsequent analysis.

Stimulation. Optic chiasm (OX) stimulation was accomplished using twisted bipolar electrodes and a Grass 58 stimulator. Stainless steel, teflon insulated wire was carefully wound into a bipolar electrode (tip diameter 0.5 mm, vertical separation 2.5 cm) and implanted in the optic chiasm (A 14.5 mm, L 2.0 mm) (Snider & Niemer, 1961). Permanent implantation followed physiological confirmation of chiasm placement.

Recording Procedures

General. On each recording day the animal was sedated but not anesthetized with a combination of acepromazine maleate (2.9 mg/kg) and sodium pentobarbital (5mg/kg). Under this sedation, unrestrained animals remained capable of feeding and ataxic locomotion. Mounting in the stereotaxic plane was effected using the previously implanted cranial bolts. Both corneas were protected with zero power contact lenses. Microelectrode placement in the LGN was achieved using standard Horsley-Clarke techniques. The dura overlying the LGN remained intact until the first electrode penetration. At this time, the meninges were manually reflected permitting unimpeded passage of the electrode.

Following procedures set forth by Fernald and Chase (1971), the position of the optic disc of the immobile left eye was plotted on a tangent screen located one meter from the orbit. Receptive field positions of LGN cells driven by the immobile left eye were located on this screen and their position relative to the projection of the optic disc was measured.

Receptive field locations were estimated for cells in layer A_1 connected to the mobile, right eye. This was possible since it is known that LGN cells are in register between geniculate layers (Bishop, Kozak, Levick, & Vakkur, 1962; Sanderson, 1971b; Kaas, Guillery, & Allman,

1972). That is, if appropriately oriented penetrations are made in the right LGN, cells located in the A_1 layers (innervated by the mobile, right eye) have homonymous retinal field locations relative to the layers A&C receiving input from the paralyzed left eye (Bishop, Kozak, Levick, & Vakkur, 1962). Thus knowledge of the receptive field locations for cells located in layers A&C innervated by the paralyzed eye provides the basis for estimation of location of fields for cells in layer A_1, innervated by the mobile eye.

All receptive fields of the LGN cells receiving afferents from the paralyzed eye were plotted. However, since previous reports on the effects of monocular paralysis have looked only at those cells within the central ten degrees, the present study analyzed only those cells within that area. Verification that the isolated units are LGN cell bodies and not fibers followed the criteria set forth by Hubel (1960) and Bishop, Burke, and Davis (1962).

To insure adequate cell sampling, no penetration was made at the same coordinates in any single cat. Each pass was at least 0.2 mm away from every other penetration.

<u>OX latency measurement</u>. Optic chiasm (OX) latency is defined as the length of time between electrical stimulation of the optic chiasm and the response to this stimulation as recorded extracellularly in cells of the

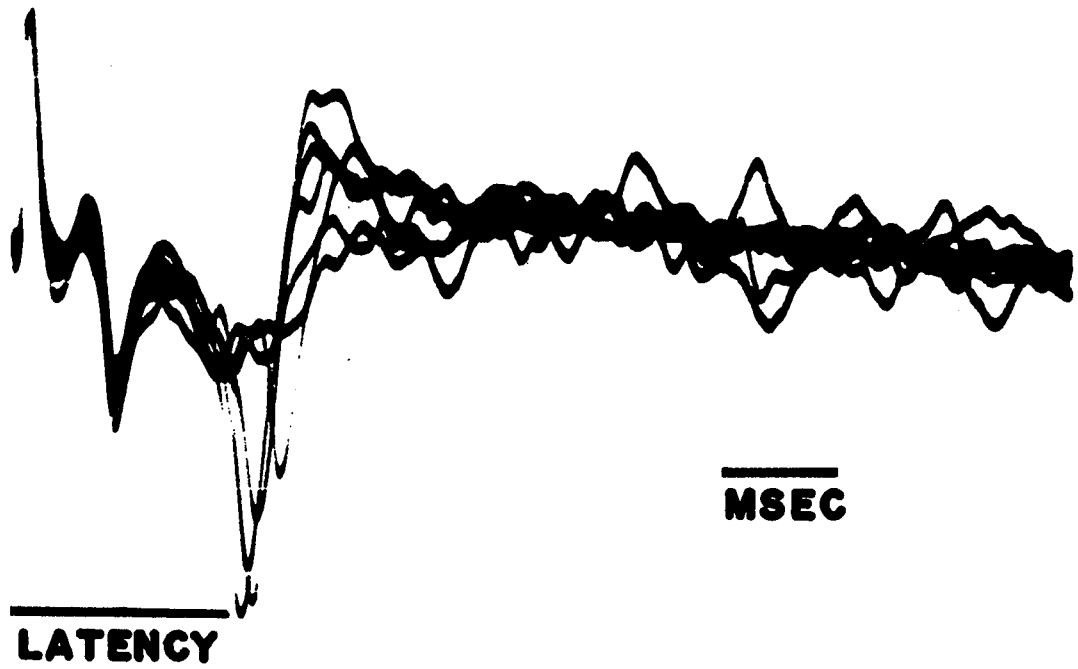
right LGN. Cell isolation and determination of cell latency proceeded as follows. During each penetration through the geniculate a Grass PS2 photostimulator steadily flashed before the cat's eyes. This visual stimulation excited visual cells in the LGN and permitted testing for ocular dominance. Ocular dominance reveals from which eye the cell receives input and consequently the layer of the LGN through which the electrode is passing. The response of geniculate cells to this stimulation was heard through a loudspeaker and observed with an oscilloscope. Isolation of a single cell (according to the criteria of Hubel [1960] and Bishop, Burke, and Davis [1962]), was immediately followed by a determination of receptive field location (immobile eye only). Following this measurement, the isolated cell was stimulated by shocks from the OX electrode. Through manipulation of the frequency, duration, and voltage parameters of the electrical shock, a reliable latency for any single cell was found. However, precise determination of firing latency was somewhat hampered by the physiological limitations of the system. A neuron doesn't necessarily fire to each shock at near threshold intensity. OX shocks, of necessity, were of low intensity since the subject was neither anesthetized nor paralyzed systemically, and high intensity shocks might cause (through current spread) movements resulting in loss of the cell. Careful manipulation of the shock parameters,

however, did permit consistent visualization of OX latencies permitting reliable latency measurement.

A further problem was posed by the variability of the cell latencies. Each cell does not fire consistently at precisely the same latency after each shock. This variability, once the stimulation parameters are locked in, was rarely more than 0.1 msec. To overcome this inherent variability, presumably arising in the synaptic processes linking optic tract fibers to LGN cells, several traces of the cell wave form were permitted to superimpose on the oscilloscope screen and stored temporarily. Figure 1 is an unretouched reproduction of several superimposed traces of the response to OX shock of a typical LGN cell. The weighted average onset latency of these several traces was estimated after the technique described by Hoffman, Stone, and Sherman (1972).

Since latency of cell response to OX stimulation was estimated, estimator reliability was of considerable interest. To evaluate this as a source of error, 71% (390/550 cells) of the latency readings were independently observed and recorded by two experimenters. Of this 390, the same latency was determined by both observers in 355 cases. Thus 91% of the time two observers agreed as to the latency judgment. Of the 35 (8%) cases in which the observers disagreed as to the latency, the margin of disagreement was never more than ±0.1 msec.

Figure 1. Sample trace of the spike responses of a lateral geniculate cell to optic chiasm (OX) stimulation. The spikes are superimposed on the geniculate field potential. Latency of any particular cell is determined by estimating the weighted onset latency of the cell.


MSEC
LATENCY

CHAPTER III

RESULTS

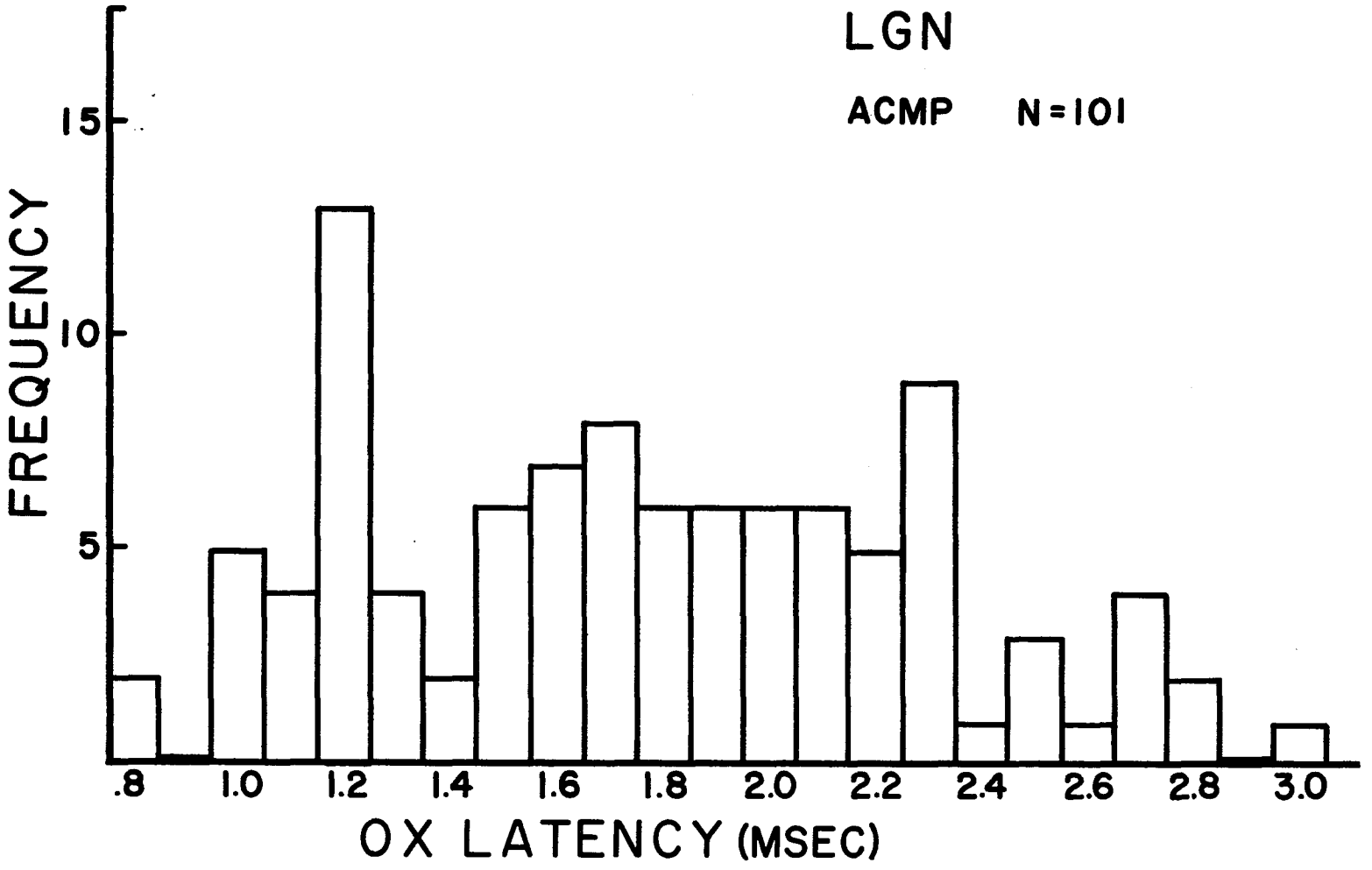
Experiment I. The Effects of Chronic Monocular Paralysis on the OX Latency Distribution of Cells in the Lateral Geniculate Nucleus

This study compared the OX latency distributions of LGN cells recorded in ACMP (acute monocularly paralyzed, eyes open; paralysis of four days or less) and CHMP (chronic monocularly paralyzed, eyes open; paralysis of fourteen days or more) animals.

Figure 2 is a frequency histogram representing the latencies of 101 cells recorded in the right geniculate of four ACMP cats. The distribution is similar to that reported by Hoffman, Stone, and Sherman (1972) for systemically paralyzed subjects in that both the distributions peak at 1.2 msec and 1.7 msec, with a trough at 1.4 msec (trough at 1.5 msec in Hoffman, Stone, and Sherman). A third peak (not evident in Hoffman, Stone, and Sherman) at 2.3 msec is seen in Figure 2, suggesting the presence of a slightly greater proportion of long latency cells as compared to the Hoffman, Stone, and Sherman report. This discrepancy may simply reflect the small sample size of the present study.

In the aggregate, the pattern of results is consistent with that obtained by Hoffman, Stone, and Sherman (1972).

Figure 2. Frequency distribution for latencies of response to optic chiasm shock (OX latency) of cells in the right lateral geniculate nucleus. Recordings are from the A_1 layer receiving input from the mobile eye and from the A&C layers receiving input from the paralyzed eye of four animals with acute monocular paralysis, eyes open (ACMP).

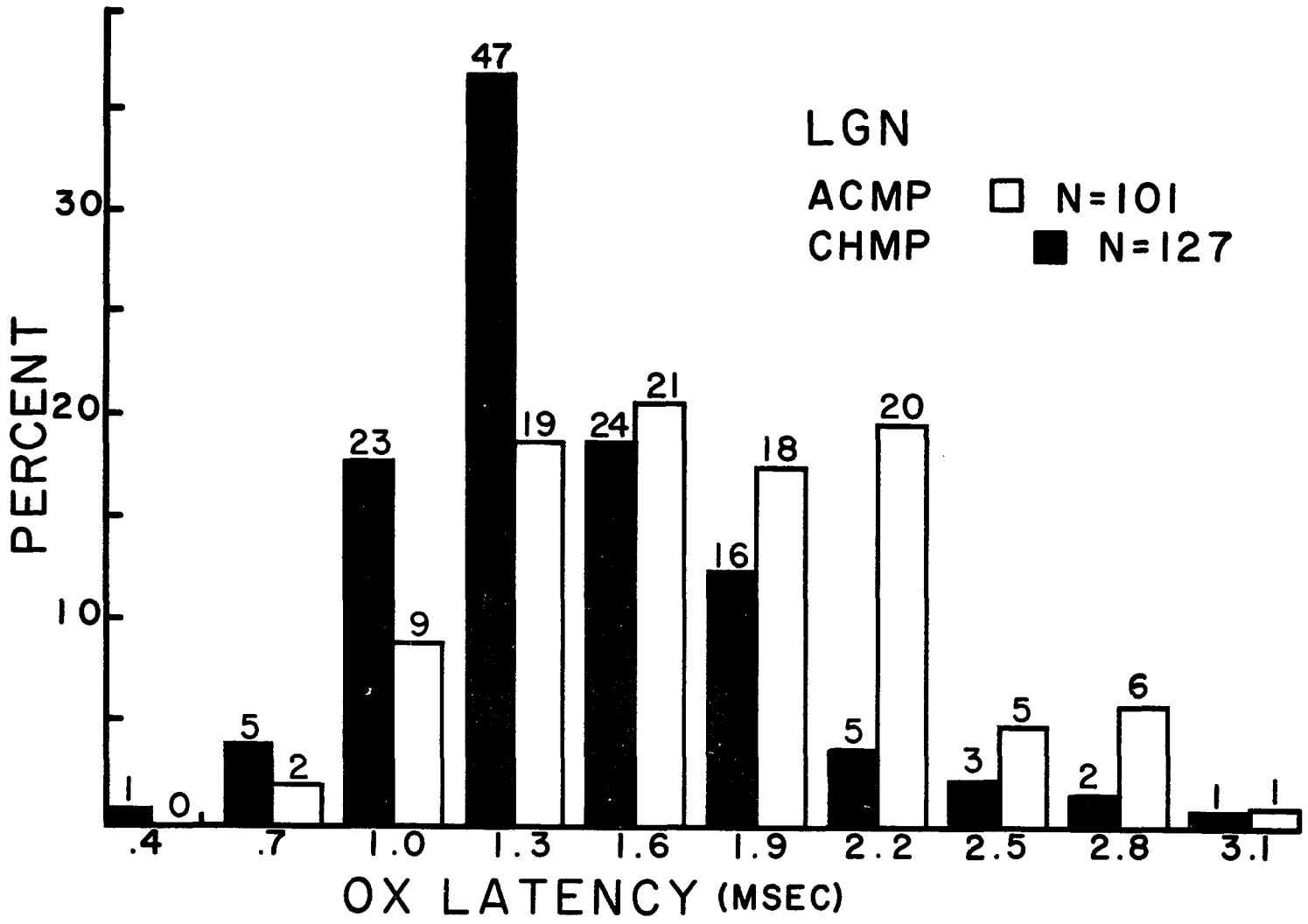

LGN
ACMP N=101
FREQUENCY
15
10
5
.8
1.0
1.2
1.4
1.6
1.8
2.0
2.2
2.4
2.6
2.8
3.0
OX LATENCY (MSEC)

This consistency suggests acute monocular paralysis has no detectable effects on the OX latency distributions of geniculate cells. As measured by distribution of OX latencies, therefore, the ACMP preparation can be regarded as normal.

The distribution of cells recorded in layers A, A_1 & C of the geniculate for four ACMP and four CHMP animals is presented in Figure 3. In this and remaining figures, the cell frequencies are expressed as a percentage of the total number of cells recorded in that condition. Cell frequencies for each latency bin are indicated by the number above the bar. Each bin includes cells recorded within 0.1 msec above and below the indicated latency.

Examination of Figure 3 reveals that ACMP and CHMP animals differ in several respects. First, mean OX latency for the ACMP animals is 1.8 msec, while that of the CHMP group is 1.4 msec. Using 20 mm as the distance from the optic chiasm to the geniculate, and assuming a synaptic delay of 0.75 msec (Hoffman, Stone, & Sherman, 1972), these latency differences can be transformed to differences in conduction velocities. For the ACMP group the mean conduction velocity calculated is 19 meters/second, while for the CHMP group the mean conduction velocity is 30 meters/second. A second difference is found in comparing the relative frequency of cells with latencies from 1.5 msec to 3.1 msec. This comparison shows that the CHMP

Figure 3. Frequency distribution for latencies of response to optic chiasm shock (OX latency) of cells in the right lateral geniculate nucleus. Recordings are from the A_1 layer receiving input from the mobile eye and from the A&C layers receiving input from the paralyzed eye of eight animals; four with acute monocular paralysis, eyes open (ACMP) and four with chronic monocular paralysis, eyes open (CHMP). Bins include units recorded at indicated latency plus or minus 0.1 msec. Number above each bin is the total of units recorded; ordinate represents percentage recorded.

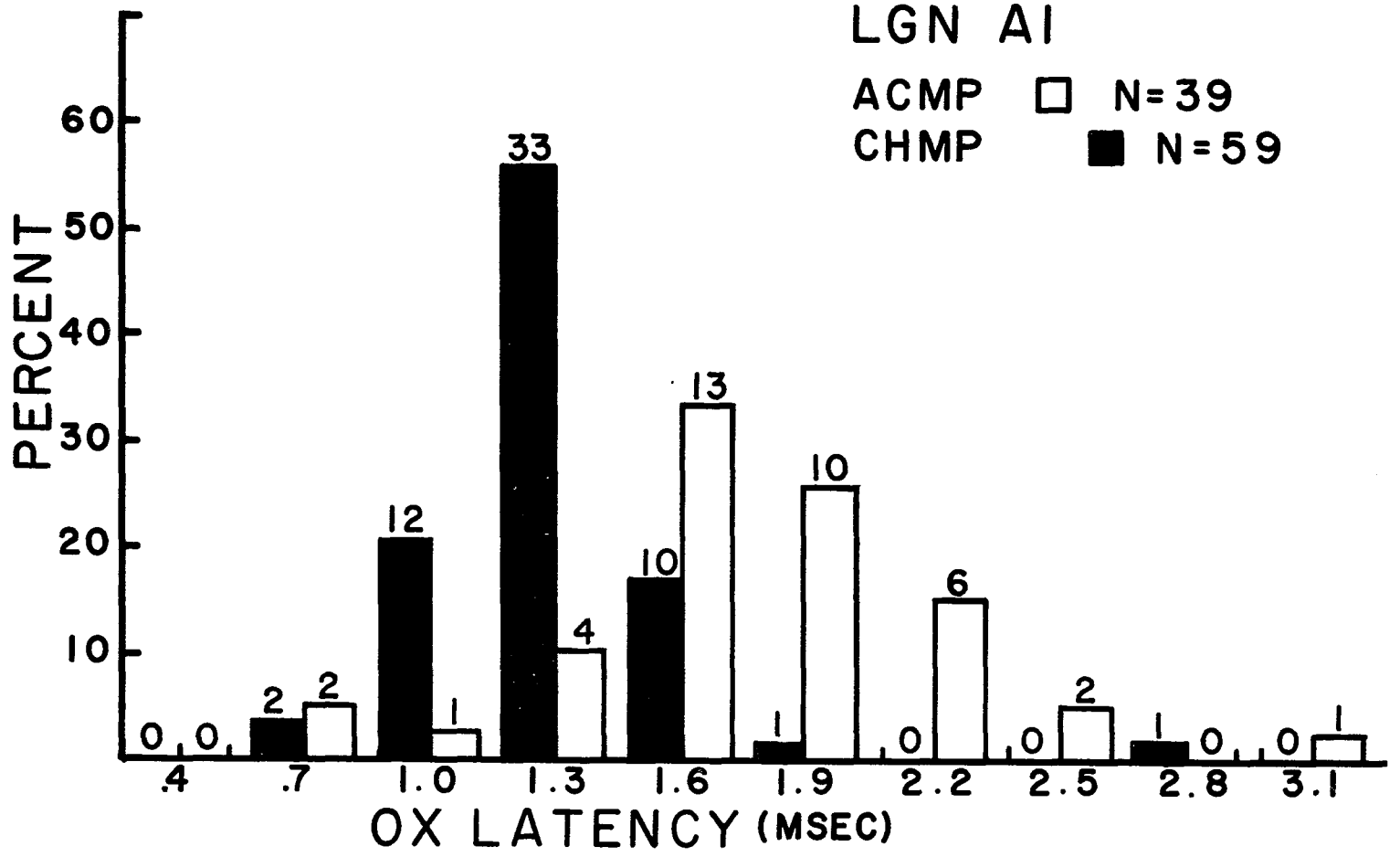

LGN
ACMP N=101
CHMP N=127
PERCENT
30
20
10
47
23
24
21
20
19
18
16
9
5
2
1
0
5
3
5
2
6
1
1
.4
.7
1.0
1.3
1.6
1.9
2.2
2.5
2.8
3.1
OX LATENCY (MSEC)

animals exhibited a smaller percentage (40%) of long latency cells than ACMP animals (70%). Correspondingly, the CHMP subjects had a larger percentage of shorter latency cells in the bins labeled 0.4 to 1.3 msec (CHMP 60%; ACMP 30%). These differences in the distributions are statistically significant ($p < .001$) (Kolmogorov-Smirnov; Siegel, 1956).

Since the latencies recorded in the ACMP preparation are comparable to those reported for systemically paralyzed animals (Hoffman, Stone, & Sherman, 1972) and are thus essentially normal, the observed differences between ACMP and CHMP animals seem attributable to the difference in duration of the monocular paralysis rather than the presence of the paralysis per se. That is, the paralysis must be maintained for a period of time greater than 4 and less than 14 days to produce the abnormal distribution of cells in geniculate.

The effect of chronic monocular paralysis on the LGN, manifested by changes in the distribution of OX latencies, may also be examined separately for the geniculate layers receiving input from the mobile and paralyzed eyes respectively. Figure 4 presents the distributions of latencies recorded from cells in the right LGN layer A_1 receiving input from the mobile, right eye. For the ACMP animals the mean latency of 39 cells is 1.8 msec (conduction velocity $\simeq$ 19 meters/sec), while for the CHMP animals the

Figure 4. Frequency distribution for latencies of response to optic chiasm shock (OX latency) cells in the right lateral geniculate nucleus. Recordings are from the A_1 layer receiving input from the mobile eye of eight animals; four with acute monocular paralysis, eyes open (ACMP) and four with chronic monocular paralysis, eyes open (CHMP). Bins include units recorded at indicated latency plus or minus 0.1 msec. Number above each bin is the total of units recorded; ordinate represents percentage recorded.

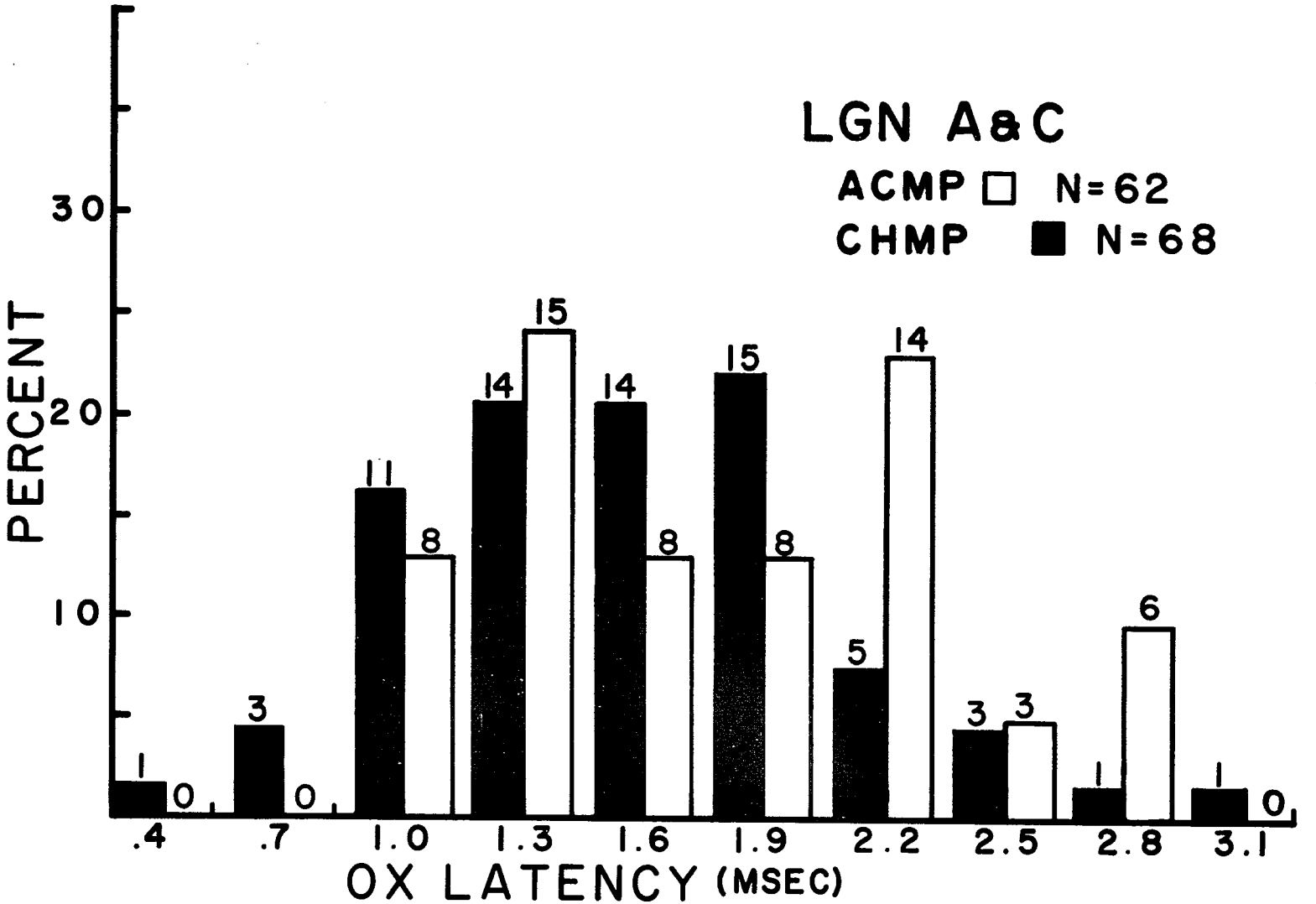

LGN AI
ACMP N=39
CHMP N=59
PERCENT
60
50
40
30
20
10
0 0 2 2 12 1 33 4 10 13 1 10 0 6 0 2 1 0 0 1
.4 .7 1.0 1.3 1.6 1.9 2.2 2.5 2.8 3.1
OX LATENCY (MSEC)

mean latency of 59 cells is 1.3 msec (conduction velocity = 36 meters/sec). The CHMP group is characterized by a lesser proportion of long latency cells (right half of the figure), and a greater percentage of shorter latency cells (left half of the figure) than the ACMP group. A convenient point for examining the differences in distributions of cells is at 1.6 msec. To the right of this point (representing cells with longer latencies), CHMP animals exhibit a smaller percentage of cells (10%) than do the ACMP animals (74%). Whereas, to the left of this point, the CHMP animals have a greater proportion of short latency cells. These differences are significant ($p < .001$, Kolmogorov-Smirnov), and indicate that chronic monocular paralysis is followed by a significant loss of longer latency cells and a corresponding gain in short latency cells in the right LGN layer (A_1) which receives afferents from the normal right eye.

Inspection of Table 2 for individual ACMP cats and Table 4 for individual CHMP cats presented in Appendix 1 suggests that the data from individual cats are not inconsistent with grouped data presented here.

The distribution of OX latencies recorded in geniculate layers A&C receiving afferents from the paralyzed left eye is presented in Figure 5. For the ACMP group the mean latency of 62 cells equals 1.8 msec (conduction velocity $\cong$ 19 meters/sec), while for the CHMP group the

Figure 5. Frequency distribution for latencies of response to optic chiasm shock (OX latency) of cells in the right lateral geniculate nucleus. Recordings are from the A&C layer receiving input from the paralyzed eye of eight animals; four with acute monocular paralysis, eyes open (ACMP) and four with chronic monocular paralysis, eyes open (CHMP). Bins include units recorded at indicated latency plus or minus 0.1 msec. Number above each bin is the total of units recorded; ordinate represents percentage recorded.


LGN A&C
ACMP □ N=62
CHMP ■ N=68
PERCENT
30
20
10
1
0
3
0
11
8
14
15
14
8
15
8
5
14
3
3
1
6
1
0
.4
.7
1.0
1.3
1.6
1.9
2.2
2.5
2.8
3.1
OX LATENCY (MSEC)

mean latency of 68 cells is 1.6 msec (conduction velocity ≅ 23 meters/sec). The ACMP and CHMP preparations appear to diverge above and below a latency of approximately 2.0 msec. At latencies longer than this, comparatively fewer cells are recorded in the CHMP group (CHMP = 15%; ACMP = 37%); at shorter latencies, more cells are recorded in the CHMP group. The distributions are significantly different ($p < .05$, Kolmogorov-Smirnov) reflecting a proportionate loss of long latency cells and a concomitant gain in the proportion of short latency cells in the CHMP preparation. Again, the individual data presented in Appendix 1 indicate that the grouped data are representative of results for individual ACMP (Table A) and CHMP (Table C) cats.

Comparison of Figures 4 and 5 reveals that the CHMP animals differ from the ACMP animals with respect to cells innervated by the mobile, right eye as well as those innervated by the paralyzed, left eye. In both cases, the distribution of cells in the CHMP group is shifted toward shorter latencies. However, the distribution shifts following chronic monocular paralysis are greater in the layer receiving from the mobile, right eye. In the ACMP preparation the mean OX latency in A_1 and A&C are identical (1.8 msec, Kolmogorov-Smirnov, $p > .10$), while the mean latency of A_1 is shorter than the mean latency of A&C

(1.3 versus 1.6 msec, Kolmogorov-Smirnov, $p < .001$) after chronic monocular paralysis.

In summary, Experiment 1 suggests that: (1) ACMP animals have LGN's with OX latency distributions that are essentially the same as animals without surgical eye paralysis, and as such may be considered normal, (2) comparison of latencies generated by ACMP and CHMP animals for layers A, A_1 & C of the right geniculate reveals a shift toward shorter latencies with a decreased proportion of long latency cells in the CHMP preparation, (3) these differences between ACMP and CHMP animals are evident in layers receiving from the paralyzed and mobile eyes, respectively, but are most pronounced in the layer receiving input from the unoperated, mobile eye, (4) in any one condition, no one cat is responsible for the effect attributed to the duration of paralysis since grouped data are representative of results for individual cats.

Experiment II. The Effect of Patterned Visual Deprivation on the OX Latency Distribution of Cells in the Lateral Geniculate Nucleus

This study compared the OX latency distributions of geniculate cells obtained from ACMP animals to those obtained from ACMP/BISUT animals (acute monocular paralysis, eyes closed for two weeks prior to recording). Differences between the two groups are taken to be the result of two weeks of patterned visual deprivation since acute monocular

paralysis itself has no effect on OX latency distributions and is common to both groups.

A comparison of latencies recorded in the right geniculate layers A&C receiving input from the contralateral eye in ACMP (n = 62) and ACMP/BISUT (n = 106) animals is depicted in Figure 6. The mean cell latency for both groups is 1.8 msec. A Kolmogorov-Smirnov test for differences in distribution and central tendency failed to reach statistical significance ($p > .10$). These results indicate that chronic patterned visual deprivation has no consistent effect on the geniculate layers A&C receiving afferents from the contralateral eye.

The distribution of cells recorded in the right layer A_1 receiving input from the ipsilateral eye for ACMP and ACMP/BISUT animals is pictured in Figure 7. The mean cell latency for the ACMP animals is 1.8 msec (n = 39), while that for the ACMP/BISUT group is 1.5 msec (n = 74). The distributions begin to diverge at the interval labeled 1.6 msec. To the right of this point, ACMP/BISUT subjects show a diminished proportion (24%) of long latency cells when compared to the ACMP group (62%). Correspondingly, to the left of this point, the ACMP/BISUT subjects show a larger percentage of short latency cells. These differences are significant ($p < .001$, Kolmogorov-Smirnov) suggesting that chronic (fourteen days or more) lack of patterned visual input produces a loss in the proportion of

Figure 6. Frequency distribution for latencies of response to optic chiasm shock (OX latency) of cells in the right lateral geniculate nucleus. Recordings are from layers A&C receiving input from the contralateral eye. The unshaded bars represent units recorded in four acute monocularly paralyzed, eyes open (ACMP) animals. The shaded bars represent units recorded in three animals prepared with the acute monocular paralysis, eyes closed (ACMP/BISUT). Bins include units recorded at indicated latency plus or minus 0.1 msec. Number above each bin is the total of units recorded; ordinate represents percentage recorded.

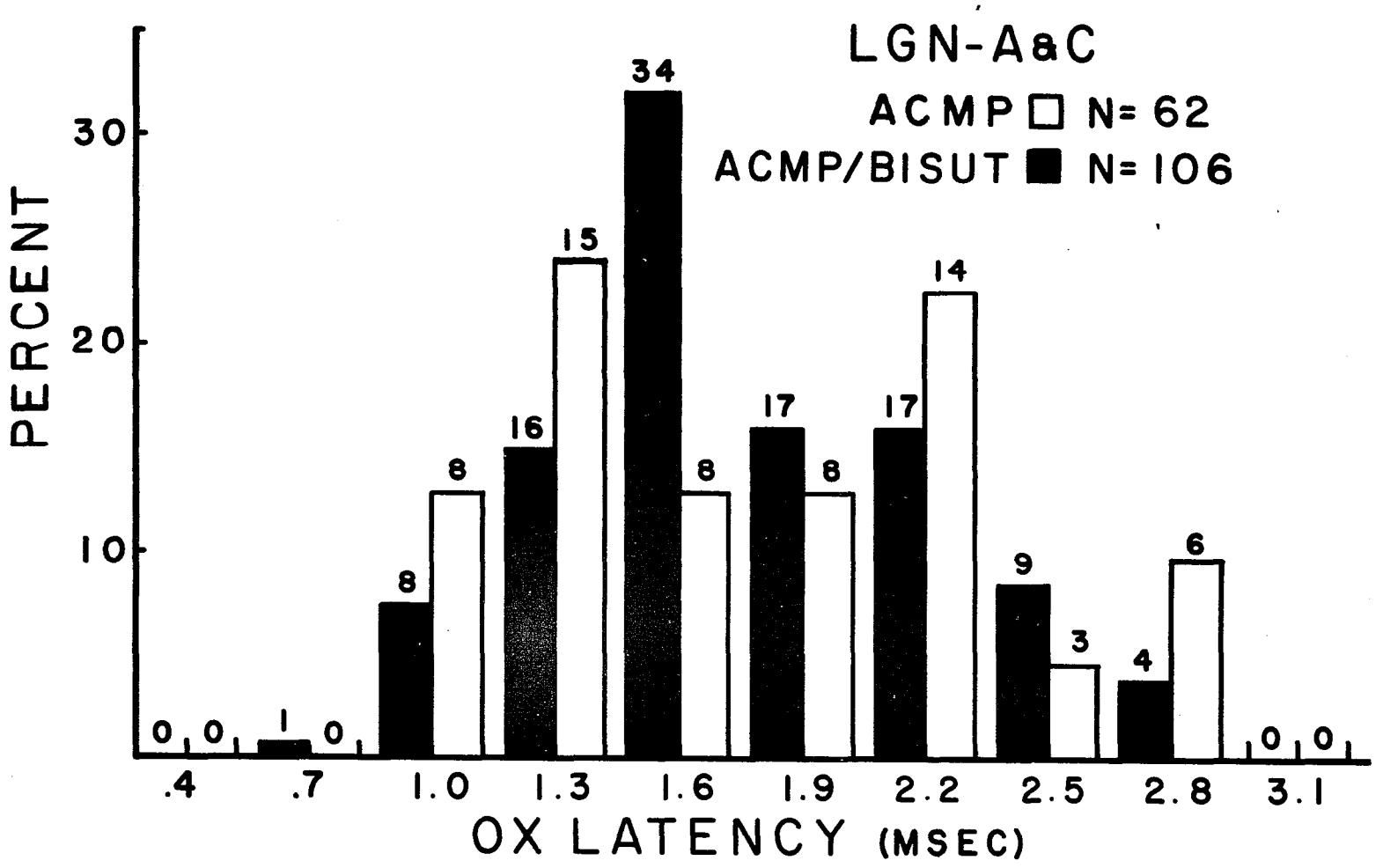
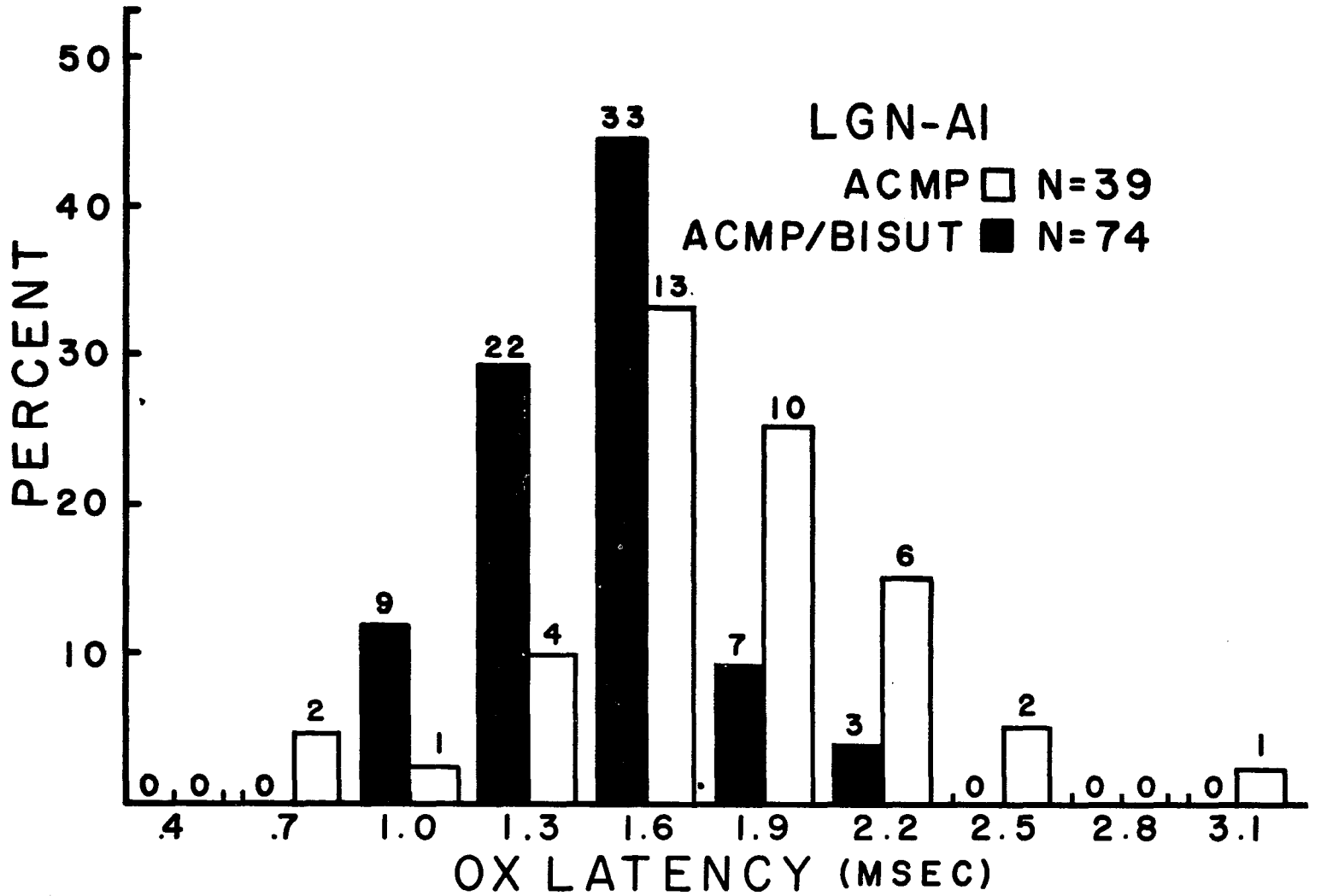

LGN-A&C
ACMP □ N= 62
ACMP/BISUT ■ N= 106
PERCENT
30
20
10
0 0 1 0 8 8 16 15 34 8 17 8 17 14 9 3 4 6 0 0
.4 .7 1.0 1.3 1.6 1.9 2.2 2.5 2.8 3.1
OX LATENCY (MSEC)

Figure 7. Frequency distribution for latencies of response to optic chiasm shock (OX latency) of cells in the right lateral geniculate nucleus. Recordings are from layer A_1 receiving input from the ipsilateral eye. The unshaded bars represent units recorded in four animals with acute monocular paralysis, eyes open (ACMP). The shaded bars represent units recorded in three animals prepared with acute monocular paralysis, eyes closed (ACMP/BISUT). Bins include units recorded at indicated latency plus or minus 0.1 msec. Number above each bin is the total of units recorded; ordinate represents percentage recorded.


LGN-AI
ACMP □ N=39
ACMP/BISUT ■ N=74
PERCENT
50
40
30
20
10
0 0 0 2 9 1 22 4 33 13 7 10 3 6 0 2 0 0 0 1
.4 .7 1.0 1.3 1.6 1.9 2.2 2.5 2.8 3.1
OX LATENCY (MSEC)

long latency cells and a gain of short latency cells recorded in the right geniculate layer A_1 innervated by the ipsilateral eye. Inspection of Table F presented in Appendix 1 indicates that the grouped data are representative of results for individual cats.

Further comparisons, between the OX latency distributions from ACMP/BISUT (Figure 7) and CHMP (Figure 4) animals suggest that in the right layer A_1 innervated by the ipsilateral eye (mobile eye in CHMP animals; lid suture only eye in ACMP/BISUT animals) chronic bilateral lid suture initiates a smaller loss in the proportion of long latency cells than does chronic monocular paralysis. For the CHMP group only 20% of the cells recorded have latencies between 1.5 msec and 3.0 msec, while for the ACMP/BISUT group 58% of the cells recorded have latencies between 1.5 and 3.0 msec. This result can also be seen by comparing the OX latency means between the two groups (CHMP, $n = 59$, $\bar{X} = 1.3$ msec; ACMP/BISUT, $n = 74$, $\bar{X} = 1.5$ msec). The Kolmogorov-Smirnov test for differences in distribution shape and central tendency is significant ($p < .001$). Thus, in the A_1 layer, it can be seen that bilateral eyelid suture has a less devastating effect than chronic monocular paralysis.

Comparisons similar to the above but for layers A&C innervated by the contralateral eye are unnecessary since no shift in the proportion of long and short latency cells

following chronic bilateral eyelid suture was found in those layers (Kolmogorov-Smirnov, $p > .10$).

In brief, the second experiment demonstrated the effectiveness of chronic pattern deprivation in producing a shift toward shorter OX latencies. This effect was, however, evident only in the right geniculate layer A_1 which receives input from the ipsilateral eye. Cells in the A&C layers of the LGN receiving afferents from the contralateral eye were apparently not affected by bilateral lid suture. Further, chronic patterned visual deprivation appears to be less damaging to the A_1 ipsilateral geniculate layer (innervated by normal eye in CHMP animals) than does chronic monocular paralysis.

Experiment III. The Role of Patterned Visual Exposure in Producing the Effects of Monocular Paralysis

This study investigates the relative contribution of retinally mediated and extraretinally mediated input to the occurrence of the monocular paralysis effect observed in Experiment I. This is accomplished by preventing all patterned visual input during the period of chronic monocular paralysis. In order to assess the capability of monocular paralysis to effect a change in the geniculate cell population without patterned visual input, a comparison was made between the distribution of OX latencies recorded in ACMP/BISUT and CHMP/BISUT animals. In this study, both groups of animals are prepared in the same way as

Experiment I except neither group is permitted patterned visual input. The ACMP/BISUT animals have both eyes sutured closed two weeks prior to paralysis surgery and recording, and the CHMP/BISUT group undergoes monocular paralysis and bilateral eyelid suture two weeks prior to recording. Thus the deprivation of patterned visual input is constant for the two groups, while the effects of the duration of paralysis are assessed.

The distributions of OX latencies, recorded in the right geniculate layer A_1 receiving afferents from the normal eye for the ACMP/BISUT and CHMP/BISUT subjects are depicted in Figure 8. Mean cell latency for both the ACMP/BISUT ($n = 74$) and CHMP/BISUT ($n = 45$) groups is 1.5 msec. No significant differences exist between the two distributions ($p > .50$, Kolmogorov-Smirnov) indicating that, without patterned visual input, monocular paralysis does not differentially affect the LGN cell population in the layer deriving input from the normal eye.

The effect of chronic paralysis without patterned visual input on LGN layers A&C innervated by the paralyzed eye is shown in Figure 9. This figure compares the OX latency distributions for animals with acute monocular paralysis, eyes closed (ACMP/BISUT) to those with chronic monocular paralysis, eyes closed (CHMP/BISUT). For the ACMP/BISUT animals, the mean latency of 106 cells is 1.8 msec (19 meters/sec), while for the CHMP/BISUT PREPARATION

Figure 8. Frequency distribution for latencies of response to optic chiasm shock (OX latency) of cells in the right lateral geniculate nucleus. Recordings are made from layer A_1 receiving input from the mobile eye. The unshaded bars represent units recorded in three animals with acute monocular paralysis, eyes closed (ACMP/BISUT). The shaded bars represent units recorded in four animals with chronic monocular paralysis, eyes closed (CHMP/BISUT). Bins include units recorded at indicated latency plus or minus 0.1 msec. Number above each bin is the total of units recorded; ordinate represents percentage recorded.

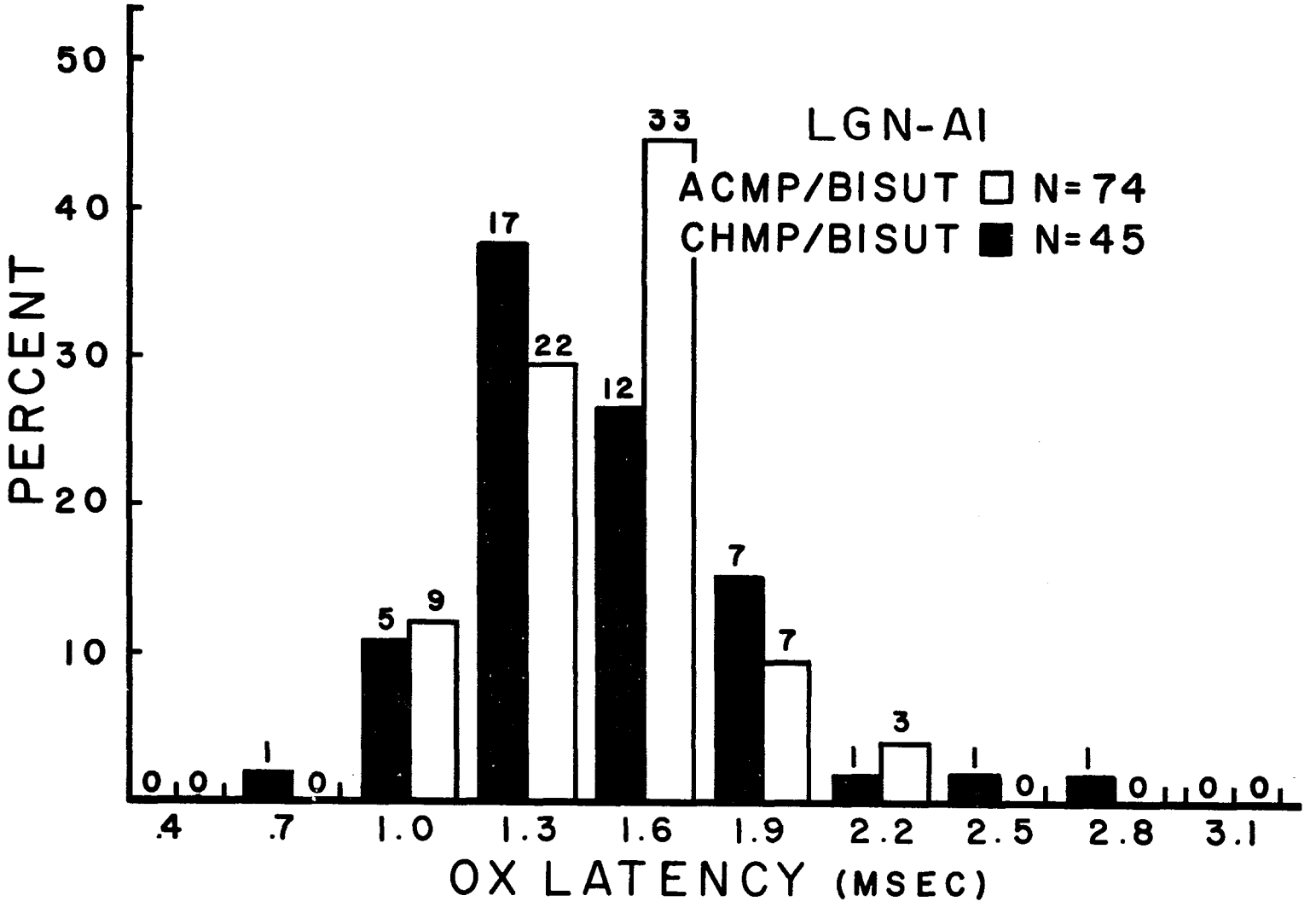
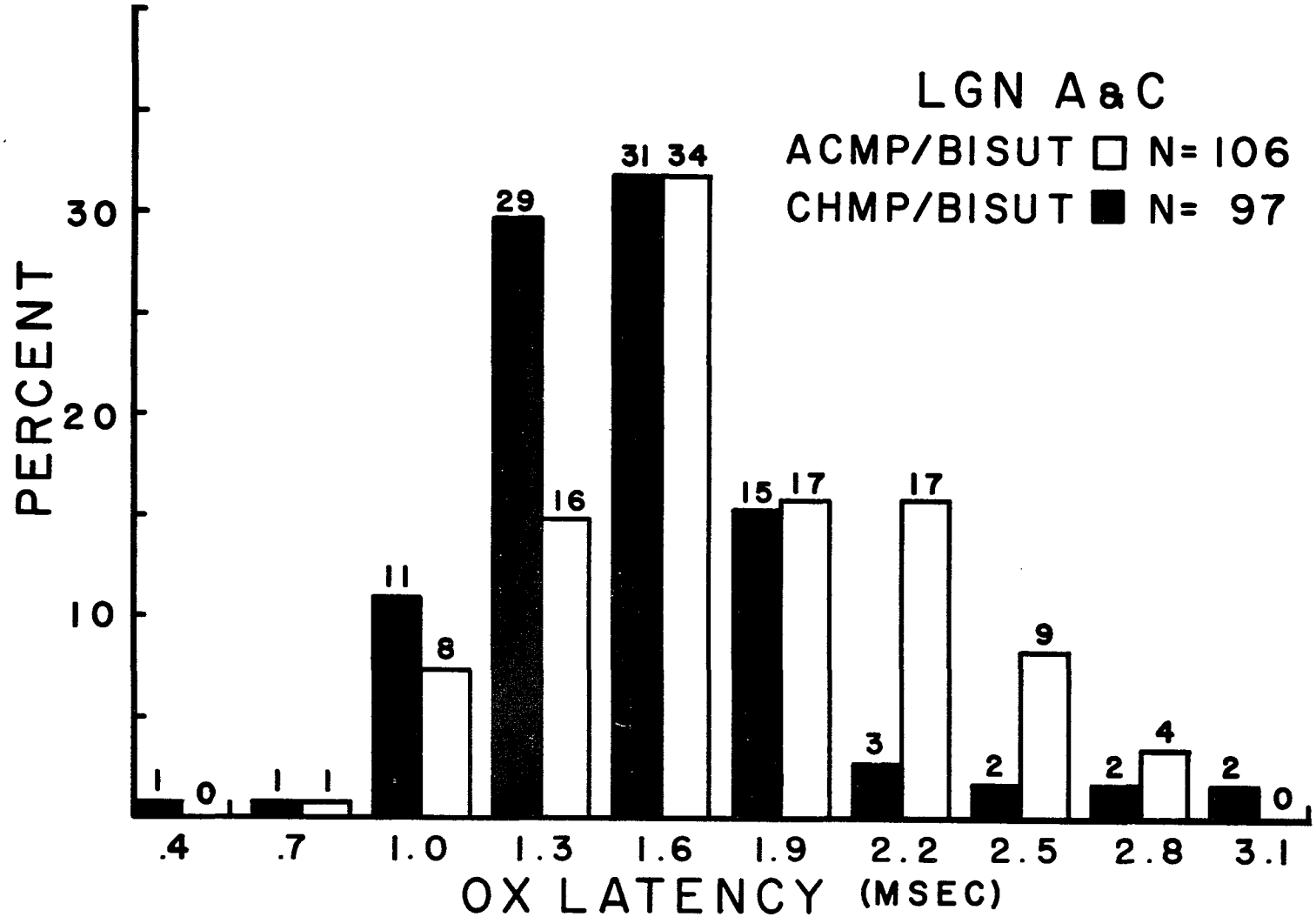

LGN-AI
ACMP/BISUT □ N=74
CHMP/BISUT ■ N=45
PERCENT
50
40
30
20
10
0 0 1 0 5 9 17 22 12 33 7 7 1 3 1 0 1 0 0 0
.4 .7 1.0 1.3 1.6 1.9 2.2 2.5 2.8 3.1
OX LATENCY (MSEC)

Figure 9. Frequency distribution for latencies of response to optic chiasm shock (OX latency) of cells in the right lateral geniculate nucleus. Recordings are made from layer A&C receiving input from the paralyzed eye. The unshaded bars represent units recorded in three animals with acute monocular paralysis, eyes closed (ACMP/BISUT). The shaded bars represent units recorded in four animals with chronic monocular paralysis, eyes closed (CHMP/BISUT). Bins include units recorded at indicated latency plus or minus 0.1 msec. Number above each bin is the total of units recorded; ordinate represents percentage recorded.


LGN A&C
ACMP/BISUT □ N= 106
CHMP/BISUT ■ N= 97
PERCENT
30
20
10
1 0 1 1 11 8 29 16 31 34 15 17 3 17 2 9 2 4 2 0
.4 .7 1.0 1.3 1.6 1.9 2.2 2.5 2.8 3.1
OX LATENCY (MSEC)

the mean latency of 97 cells is 1.6 msec (24 meters/sec). Figure 9 shows that to the right of the latency bin labeled 1.6 msec, there is a smaller percentage of cells in the CHMP/BISUT group (CHMP/BISUT = 57%; ACMP/BISUT = 76%). Correspondingly, to the left there is a greater percentage of shorter latency cells recorded in the CHMP/BISUT subjects. The Kolmogorov-Smirnov test for differences in distribution shape and central tendency is significant ($p < .01$). This suggests that even without patterned visual input there is a loss of long and a gain of short latency cells in the LGN layers connected to the immobile eye.

In review: (1) results of Experiment I indicate an overall shift in OX latencies toward shorter values in geniculate cells following monocular paralysis. The shift is more extensive in the lamina innervated by the normal eye. (2) Experiment II indicates a shift similar to that produced by monocular paralysis occurs in the right geniculate layer A_1 receiving input from the right eye as a result of bilateral eye lid closure alone. (3) Experiment III shows that the changes in latency distributions following chronic monocular paralysis are accounted for differently in the LGN laminae. Since deprivation of patterned visual input during the chronic paralysis period does not prevent the effects of monocular paralysis on the A&C layers, retinal mediation in the form of discordant

visual input cannot be the basis for the shift in cells observed in Experiment I for the layers A&C innervated by the paralyzed eye. In these layers the oculomotor factors account for the effect of monocular paralysis. However, since chronic monocular paralysis does not itself produce a change in OX latency distributions in layer A_1 if the animal is concurrently pattern deprived, oculomotor factors cannot account for the OX latency distribution shifts there. Rather, in that layer, retinally mediated factors account for the effects of monocular paralysis.

CHAPTER IV

DISCUSSION

The results reported here confirm and extend reports of a degree of plasticity in mammalian nervous system previously recognized only in immature organisms. Experiment I supports previous work (Brown & Salinger, 1975) which found a diminished proportion of a specific cell type is recorded in the LGN of adult animals following chronic monocular paralysis. A diminished proportion of these cells is also found in layer A_1 receiving afferents from the unoperated, continuously mobile eye. Knowledge of the plasticity evidenced by the adult visual system is further extended by observing it as a response not just to monocular paralysis but also to bilateral eyelid suture as well (Experiment II). Since the bilateral eyelid suture preparation affects retinally mediated input and not extraretinally mediated motor input, Experiment II suggests that the loss of X-cells following bilateral eyelid suture is initiated by retinally mediated factors. The results of Experiment III (chronic monocular paralysis with both eyes sutured concurrently) suggests that the distribution shifts observed in the geniculate X-cell population following monocular paralysis may be produced in response to retinally mediated stimuli in the geniculate

layer A_1 innervated by the mobile, unoperated eye, and extraretinally mediated stimuli in layers A&C innervated by the paralyzed eye.

The fact of plasticity in the adult visual system may have implications for the clinician treating visual system dysfunction, as well as for developmental neurobiology in general. Further, the results come to bear on some theories of neural connectivity in the mammalian visual system. Before detailing the possible impact of the reported studies however, one should consider possible interpretations for the observed changes in geniculate.

Fate of Geniculate X-Cells

The selective loss of LGN X-cells observed by Brown and Salinger (1975) could have been due to either atrophy or suppression of LGN X-cells such that they were recorded less frequently, or to a change in LGN X-cell receptive field properties such that they responded to visual stimuli as if they were Y-cells. Recall that the OX latency measure used in the present study permits analysis of these two alternatives.

The decreased proportion of long latency cells recorded in Experiment I appears to support the Brown and Salinger (1975) conclusion that cells atrophy or are suppressed rather than change their receptive field properties such that they respond as Y-cells. There are other ways however, in which a decreased proportion of geniculate cells

with OX latencies in the X-cell range could be achieved which would not require atrophy or suppression of long latency cells. While not probable, for the reasons expressed below, it is possible that the results indicate a gain in the absolute number of short latency cells such that they are recorded more frequently than long latency cells.

A gain in number of short latency cells recorded could occur by: (1) an increase in conduction velocity of retinal ganglion cell axons which innervated long latency LGN cells such that the long latency LGN cells become short latency LGN cells, (2) the growth of new LGN cells afferented by ganglion cells having rapid conduction times, (3) de-repression of short latency cells which are normally inactive but present in geniculate, (4) suppression of long latency cells, (5) actual loss or shrinkage of long latency LGN cells, or (6) any combination of the above.

LGN cells receive direct afferents from either X or Y retinal ganglion cell axons (Hoffman, Stone, & Sherman, 1972) and therefore the latency of LGN cell response to OX shock depends on the conduction velocity of retinal ganglion cell axons. Since retinal ganglion cells do not have access to binocular information, there is no reason to believe that retinal ganglion cell axons would change their conduction velocity (and therefore LGN cell OX latency) in response to interruptions of motor or visual

interaction precipitated by monocular paralysis or bilateral eye lid suture. Even if binocular information were available to retinal ganglion cells, to date there is no evidence in the physiological literature to suggest that neurons are capable of altering their conduction velocities, and therefore OX latencies. It is possible, however, that increases of conduction velocity exist but are unknown to current theorists. However, since normal nervous system functioning is dependent upon the precise timing of arrival and departure of electrical activity throughout the system, it seems inconceivable that such a short trauma period would be followed by such a tremendous alteration of nervous system timing relationships. Such an alteration would produce unimaginably complex functional ramifications resulting in total disruption of the system.

The growth of new short latency LGN cells (Case 2) seems remote for two reasons. Neither mitosis nor uptake of tritiated thymidine have been observed in adult mammalian brain neurons (cited in Jacobson, 1970). However, given that this cannot be completely eliminated as a possibility, a smaller proportion of recorded long latency cells could occur due to: (a) a combination of growth of new short latency LGN cells and a modification of long latency LGN cells such that they are suppressed or non-functional, (b) growth of new short latency LGN cells such that the

long latency LGN cells have been outnumbered and are recorded in smaller proportions, or (c) a combination of growth of new short latency LGN cells and death of long latency LGN cells.

If the situation is such that there is a gain due to growth of new short latency LGN cells, and the long latency LGN cells remain in the geniculate but perhaps nonfunctioning (a), then one might expect a larger than normal geniculate volume in the respective layers. The growth of new short latency LGN cells such that long latency LGN cells are recorded less frequently (b) would also suggest the development of a larger than normal geniculate volume. A combination of growth of short latency cells and death of long latency cells (c) could occur with no change in LGN volume, a diminished LGN volume, or an increased volume depending on the proportions of growth and deaths.

If either Case 3 (derepression of short latency cells) or Case 4 (suppression of long latency cells) obtains, then tissue volume might be expected to remain the same. However, if the anomalous OX latency distribution is due to a substantial loss of LGN cells with long latencies (Case 5) and not due to any of the above combinations of cell gain, change or derepression (Case 6) then one might expect a decrease in the tissue volume in the LGN layers under discussion. Postrecording histological examination of the geniculate following chronic monocular

paralysis suggests a loss of cell volume (Salinger, Ward, & Hooker, 1977).

Given the above, deviations from normal in the frequency of particular OX latencies recorded in the LGN of adult animals with monocular paralysis or bilateral eyelid suture may be attributed to the failure of individual LGN cells with those latencies to respond to visual stimuli and OX shock. This failure to record cells with particular latencies is interpreted as being due to the functional atrophy of those cells and not that the missing cells have acquired latencies in the range of Y-cells that are recorded. Thus for the purposes of this discussion, the data have been assumed to reflect a loss of long latency LGN cells rather than any of the other possible interpretations.

For the purpose of brevity, throughout the discussion, OX latency distribution shifts toward short latencies have been described in terms of an X-cell loss. This terminology is used to describe the diminished proportion of long latency LGN cells recorded following monocular paralysis or bilateral eyelid suture and is not based on receptive field analysis of the LGN cell population.

Functional Mechanism for X-Cell Loss Following Either Monocular Paralysis or Bilateral Eyelid Suture

The loss of LGN X-cells observed following monocular paralysis or bilateral eyelid suture may be accounted for differently in layers A&C and A_1. The A_1 layer appears

primarily sensitive to retinally mediated factors so that losses are observed following either chronic monocular paralysis or bilateral eyelid suture; whereas, layers A&C are more sensitive to extraretinally mediated factors with losses observed there due to monocular paralysis even in the absence of patterned visual input. The possible functional mechanisms underlying the influence of these two factors on cells in the LGN are discussed in this section. Possible explanations for the selective (why X and not Y) cell loss are discussed later.

Extraretinally Mediated Factors

Experiment III assessed the contribution of extraretinally mediated factors to the loss of X-cells associated with monocular paralysis by eliminating the possible effects of retinally mediated visual input. That is, comparisons were made between OX latency distributions of animals with acute monocular paralysis and bilateral eyelid suture (ACMP/BISUT) and animals with chronic monocular paralysis and bilateral eyelid suture (CHMP/BISUT). This comparison holds the effects of bilateral eyelid suture constant (since both groups are bilaterally eyelid sutured) while assessing the effectiveness of monocular paralysis in initiating a geniculate change without patterned retinal input. The results indicated that even without benefit of pattern vision, there is a functional loss of long latency cells which may be attributed to the paralysis, but only in

LGN layers A&C. Such a cell loss in chronically paralyzed animals denied patterned visual input during paralysis suggests that discordant visual input is not a factor. Rather, the disruption of a second system, one not involved with processing of retinal information, is responsible. This second system would be the oculomotor system or some related system which has powerful, extraretinal inputs to the visual system.

Discordant motoric information from the two eyes can initiate the observed changes in LGN layers A&C if (1) eye muscles have receptors that are capable of encoding proprioceptive eye position information, (2) this nonvisual information as to eye position is transmitted to central visual centers and/or oculomotor centers dealing with muscle movement, and (3) if the geniculate receives inputs from these centers. That is, for the results reported for the A&C layers to be based on extraretinal factors, the visual system must have, either directly or perhaps indirectly via the oculomotor system, access to extraretinal afferent information regarding eye position and the geniculate must contain cells that are responsive to changes in these systems. These criteria seem to be fulfilled.

Muscle state information appears to originate in the extraocular muscle fibers (Criterion 1). Although cat extraocular muscles do not have typical muscle spindles or tendon organs, they do have structures of spiral ending form that respond to stretch (Bach-y-Rita & Ito, 1966).

There is also support for the existence of afferent muscle state information (Criterion 2) transmitted to either/or both the oculomotor system in the cerebellum (Fuchs & Kornhuber, 1969) and a central visual structure, Area 17 of striate cortex (Buisseret & Maffei, 1977).

Possible pathway for eye position input to the LGN via the cerebellum. Using evoked potential techniques, Fuchs and Kornhuber (1969) investigated afferent input to the cat cerebellum from extraocular muscles. They found short latency responses in the anterior and posterior lobes of the cerebellum following manual eye muscle stretch. More recent reports have used responses from single cerebellar units to either electrical stimulation of the trochlear nerve (IV) or manual stretching of the extraocular muscles. After dissecting out the superior oblique muscle in cats, the afferent branches of the trochlear nerve were stimulated by Baker, Precht, and Llinas (1972). Their results indicated that stimulation of the trochlear afferents (previously innervating the superior oblique muscle) was followed by clear field potentials in the vermal lobules V, VI, and VII. Single unit analysis indicated Purkinje cell activation following similar stimulation of the trochlear nerve.

Similar results were obtained by Batini, Buisseret, and Kado (1974) using enucleated cats. They determined that Purkinje cells located in cerebellar lobules VI and VII

were activated by stretch applied to the lateral rectus muscle. These findings then, support the existence of afferent information to centers concerned with oculomotor integration.

Granted that eye muscle afferents project centrally, data also support the existence of eye position input to the LGN. Jeannerod and Putkonen (1970, 1971) recorded extracellularly from cells in the lateral geniculate and found 51% of the units exhibited firing rate changes time-locked with eye movements in darkness. The change in spike rate (either increase or decrease) was time-locked to after-nystagmus initiated by stimulating the vestibular nucleus. They concluded that there are cells in the geniculate that respond to oculomotor input independently of direct visual input.

Support for the existence of oculomotor input to the geniculate also comes from recording gross electrical potentials. Jeannerod and Sakai (1970) recorded the EEG in the geniculate of cats and found eye movement potentials with short latencies after the beginning of eye movements in darkness.

The above studies then, support the hypothesis that there is motoric eye position input to the geniculate which does not depend on retinal image shifts for altering response of LGN cells. It should be noted, however, that there is a conflicting report as to the activity of geniculate neurons

in response to eye movements in the absence of light. Noda and Adey (1974) have reported that, after recording 450 LGN neurons, they could not find one that exhibited a discharge rate change associated with eye movements in darkness. This finding, of course, does not support the data presented here suggesting the existence of extra-retinal afferents to the geniculate. There does not appear to be an adequate explanation for the discrepancies between this study and Jeannerod and Putkonen (1971). However, it is possible that eye movements arising in differing contexts (REM sleep, Caloric Nystagmus and spontaneously occurring) have differing physiological bases.

Possible pathway for eye position input to LGN through striate cortex. Buisseret and Maffei (1977) stimulated the extraocular muscles of adult cats and recorded in Area 17 of visual cortex. The activity of 90 binocular cortical cells were recorded during electrical stimulation of an extraocular muscle (lateral rectus, inferior oblique, superior oblique). They found that 25% of the recorded cells showed clear responses. Further, they observed that many times units responding to the stimulation of a particular muscle would not respond to similar stimulation of another muscle. It is thus possible that the low percentage of cortical cells responding to stimulation of the ocular muscle in this study may be due to the failure to stimulate the correct muscle. The Buisseret

and Maffei (1977) report thus indicates a second central route for afferent eye muscle proprioceptive information. In this instance the eye position information is routed to binocular cells in Area 17 involved in processing retinal input.

However, that extraretinal eye position information is available to binocular cortical cells does not in itself explain the effects of eye paralysis on the geniculate. A further requirement for this route to be involved in monocular paralysis affects would be that cortical cells reinnervate geniculate cells with motoric information. Several studies have, in fact, found that there is corticofugal input to the geniculate (Widen & Ajmone-Marsan, 1960; Ajmone-Marsan & Morillo, 1961; Guillery, 1967; Vastola, 1960; Kalil & Chase, 1970; Hollander, 1970; Updyke, 1975, 1977). However, whether these inputs from cortex carry motor information is unknown.

In summary, it appears that there is extraretinal information with regard to eye position transmitted both to oculomotor centers in the cerebellum and visual cortex. Further, there may be cells in the geniculate that are responsive to cortical or oculomotor influence. Although these findings do not in themselves support the hypothesis of discordant ocular motricity as the responsible factor in the loss of X-cells in the A&C laminae of the cat with monocular paralysis, they do suggest a physiological substrate on which such a hypothesis may rest.

Given the above data, it is suggested that the interruption of concordant motor information from the two eyes disrupts the normal functioning of geniculate X-cells in laminae A&C causing them to be recorded less frequently than Y-cells. The alteration of normal functioning could be followed, after a period of time, by X-cell atrophy of disuse or by X-cells that continue to remain anatomically present but functionally suppressed.

Retinally Mediated Factors

In Experiment I monocular paralysis produced a loss of LGN X-cells in the A_1 layer. Experiment II indicated that chronic pattern deprivation alone initiates a significant loss of LGN X-cells in the A_1 layer. The loss of LGN X-cells observed in Experiment II seems attributable to lack of patterned visual input (retinally mediated effects) since the effects of acute monocular paralysis are constant for both groups. In both Experiment I and Experiment II a loss of LGN X-cells indicated the effectiveness of either chronic monocular paralysis or bilateral eyelid suture in altering the geniculate.

Since monocular paralysis alone (Experiment I) and pattern deprivation alone (Experiment II) each initiate a loss of LGN X-cells in layer A_1, a comparison of OX latency distributions for ACMP/BISUT animals and CHMP/BISUT animals (Experiment III) should reveal a greater diminution of LGN X-cells in the A_1 layer of the CHMP/BISUT group than

in the ACMP/BISUT group unless the effects of chronic monocular paralysis are retinally mediated. If, however, the effects of chronic monocular paralysis in layer A_1 are retinally mediated, there should be no additional loss in the proportion of X-cells in CHMP/BISUT beyond that associated with bilateral lid suture itself, since bilateral eyelid suture prevents patterned visual input and therefore precludes retinal mediation.

Inspection of the OX latency distributions for the A_1 layer of ACMP/BISUT and CHMP/BISUT animals indicates no significant additional attrition of LGN X-cells occurs in the CHMP/BISUT animals. In contrast to Experiment I and Experiment II where a loss of LGN X-cells indicated the effectiveness of chronic monocular paralysis or bilateral eyelid suture, in Experiment III a <u>failure</u> to observe a significant loss of LGN X-cells indicates the effectiveness of bilateral eyelid suture in preventing the effects of monocular paralysis. A failure to observe a reduction in the proportion of LGN X-cells following CHMP/BISUT itself cannot be taken to mean that a definitive change in the proportion of X- and Y-cells has not occurred. It is possible that a small change has occurred that is not recorded. However, even if an undetectable distribution shift in layer A_1 occurs following CHMP/BISUT, it would be of such comparatively small magnitude to the significant distribution shift in layer A_1 following monocular paralysis

(Experiment I) that one must conclude that pattern vision is required for the effects of monocular paralysis to occur.

The failure to find a significant reduction in the proportion of X-cells following CHMP/BISUT, contrasted with the significant reduction of X-cells following monocular paralysis with eyes open, and the loss of LGN X-cells following bilateral eyelid suture, both seem attributable to a lack of patterned input caused by the bilateral eyelid closure. This suggests that in A_1, the loss of X-cells during chronic monocular paralysis without lid suture and during bilateral eyelid suture, is due to the disruption of retinally mediated factors produced by these manipulations and not to disrupted extraretinally mediated factors.

The loss of X-cells in layer A_1 observed after bilateral eyelid suture seems easily understandable in terms of abnormal retinal mediation. Bilateral lid suture prevents patterned visual input and thus may interrupt normal geniculate functioning. However, attribution of the X-cell loss observed in layer A_1 in the monocular paralysis preparation to abnormal retinal mediation is more difficult to understand. Since in the monocular paralysis preparation layer A_1 receives direct afferents only from the normal right eye, how is it that paralysis of the left eye initiates the observed selective cell loss? It is suggested that disruption of normal binocular interaction in the LGN

initiated by abnormal visual input consequent to either monocular paralysis or bilateral eyelid suture may account for the X-cell losses observed in the A_1 layer.

It is particularly appealing to be able to explain the effect of monocular paralysis and bilateral eyelid suture by the common mechanism of disrupted binocular inhibitory interaction in the geniculate. However, in the case of bilateral eyelid suture in A_1, one cannot rule out the possibility that the observed LGN losses are secondary to losses occurring in retinal X-cells. Although losses of retinal ganglion X-cells cannot be excluded in this context, it appears that binocular eyelid suture does not produce this effect but operates primarily on binocular inhibitory interaction in the geniculate. Supporting data are indirect and derived from kittens. First, eyelid suture does not affect retinal ganglion cells (Sherman & Stone, 1973). And second, bilateral eyelid suture has been observed to impair binocular inhibitory interaction in the geniculate of kittens (Sherman & Sanderson, 1972).

Until recently it has generally been accepted that little communication occurs in geniculate between afferents from the two eyes, with optic tract fibers from the contralateral retina projecting only to laminae A&C, and those from the homolateral eye to lamina A_1 (Hayhow, 1958; Guillery, 1966; Kaas, Guillery, & Allman, 1972; Hickey & Guillery, 1974). Recently, however, it has been shown that

although there is segration of the optic tract fibers into alternate geniculate layers, there does appear to be binocular interaction occurring in the geniculate (Vastola, 1960; Suzuki & Kato, 1966; Singer, 1970; Suzuki & Takahashi, 1970; Sanderson, Bishop, & Darian-Smith, 1971; Sherman & Sanderson, 1972; Fukada & Stone, 1976).

Geniculate neurons are discharged by impulses from only one eye (Sanderson, Bishop, & Darian-Smith, 1971). However, it has been found that geniculate neurons excited by light (Singer, 1970; Sanderson, Bishop, & Darian-Smith, 1971), or electrical stimulation of the optic nerve (Vastola, 1960; Suzuki & Kato, 1966; Suzuki & Takahashi, 1970) of one eye, are inhibited by similar stimulation of the other eye. It thus appears that there is some binocular interaction at the geniculate level. That this interaction can occur at the geniculate level and not just via corticofugal influences is supported by data indicating that ablating (Sanderson, Bishop, & Darian-Smith, 1971) or cooling (Singer, 1970) of the cortical sites projecting to the geniculate does not abolish binocular inhibitory interaction.

A more recent report by Schmielau and Singer (1977) supports and extends these earlier findings. They found that cortical inactivation by cooling completely abolished binocular facilitation but only partially disrupted binocular inhibition. They concluded that since binocular

inhibition is not totally abolished by cortical cooling, it depends not only on the corticothalamic pathways but also on an intrageniculate component.

Binocular interaction at the LGN level is a mechanism by which abnormal pattern vision impinging on the two eyes could affect lamina A_1 in either the monocular paralysis or bilateral eyelid suture preparations. Disruption of this binocular mechanism could form the basis for the geniculate cell loss observed in the A_1 layer.

Binocular interaction at the geniculate level may explain not only the existence of the X-cell losses in layer A_1 following monocular paralysis or bilateral eyelid suture, but also the greater cell loss seen in A_1 when compared to A&C in the monocular paralysis preparation. Suzuki and Takahashi (1970) found that binocularly inhibited cells are more commonly found in geniculate lamina A_1. Comparing the frequency of binocularly inhibited cells recorded in layers receiving from the contralateral optic nerve (A&C) and those receiving afferents from the ipsilateral optic nerve (A_1), they found that 76% (61/80) of the ipsilateral (A_1) cells and 18.5% (13/70) of the contralateral (A&C) cells were binocularly inhibited. Sanderson, Bishop, and Darian-Smith (1971) found similar results.

The apparent greater susceptibility of LGN cells receiving afferents from the ipsilateral eye to inhibiting

influences of the contralateral eye is a mechanism whereby the more dramatic loss observed following monocular paralysis in the A_1 layer may possibly be explained. Thus, it is proposed that abnormal visual input alters the normal functioning of geniculate binocular interaction in such a manner as to cause an anatomical and/or functional suppression of X-cells in layer A_1 making them less frequently recorded.

In summary, there appear to be different etiologies for the functional loss of X-cells observed in the A_1 and A&C laminae following monocular paralysis. For the A&C layers, discordant motoric input, either to cerebellar oculomotor centers or visual centers innervated by eye muscle afferents, may interrupt normal LGN cell functioning. This functional alteration could be followed by X-cell shrinkage.

For the A_1 layer, the loss of functional X-cells appears to be the result of abnormal retinal input produced by monocular paralysis or bilateral eyelid suture. Abnormal binocular interaction at the LGN level seems to account for the alteration of X-cells in this layer. Again, the alteration in normal functioning could result in X-cell shrinkage.

Possible Explanations for Selective Cell Loss--(Why X and Not Y?)

Two mechanisms may be responsible for the selective functional loss of LGN X-cells. The bases for the observed

X-cell loss is different for those layers susceptible to motoric perturbations (A&C following monocular paralysis) and the layer susceptible to abnormal visual input (A_1) following monocular paralysis or bilateral lid suture.

Layers A&C.

In the previous section, support has been presented for input of extraretinal muscle proprioceptive eye position information to both the cerebellar oculomotor system and visual cells in Area 17 of the occipital cortex and from either of these to LGN. While this permits such information to be central to monocular paralysis related cell loss, it in itself does not explain why LGN X-cells are selectively susceptible to monocular paralysis in the A&C laminae. However, if it can be demonstrated that (1) a greater proportion of LGN X- rather than LGN Y-cells project to Area 17, (2) extraretinal proprioceptive eye position information projects to Area 17, and (3) there is innervation of LGN X-cells by corticofugal fibers from Area 17, then there would be a basis for suggesting that an interaction between the motoric system and visual system occurs in the visual cortex and thus may influence the geniculate to produce the selective cell loss. Although the data are incomplete, there is evidence suggesting that the three criteria have been fulfilled.

With regard to the first criterion, there are physiological data supporting the existence of a differential termination of X- and Y-cells in Areas 17 and 18.

Stone and Dreher (1973) antidromically activated LGN cells by electrically stimulating Areas 17 and 18. They found Y-cells responded at low intensity thresholds to stimulation of both areas suggesting that Y-cells project to both areas. X-cells responded to low stimulus currents only to stimulation of Area 17. They concluded that the axons of X-cells terminate predominately or exclusively in Area 17.

Morphological evidence also supports the predominance of termination of X-cells in Area 17, and Y-cells in Area 18. Garey and Powell (1967) produced lesions in Areas 17 and 18. If the lesion was restricted to Area 17, retrograde cell degeneration occurred mainly in the small and medium size LGN cells. However, if both Areas 17 and 18 were lesioned, the degeneration in LGN cells occurred not only in the small and medium cells but also in the large geniculate cells. Thus small and medium size cells project to Area 17, while the large LGN cells project to Areas 17 and 18. Since it has been suggested that X-cells have smaller cell bodies than Y-cells (Boycott & Wassle, 1974), these results imply that X-cells project mainly to Area 17, while Y-cells project to Areas 17 and 18.

Further anatomical studies support the differential cortical termination areas for X- and Y-cells. Gilbert and Kelly (1975) and Hollander and Vanegas (1977) injected horseradish peroxidase into Areas 17 and 18. They found that after injection in Area 18, LGN cells labeled by

retrograde axonal transport were larger than cells labeled after Area 17 injections. Similar results were found by Garey and Blakemore (1977) who also suggested that LGN Y-cells innervate Area 18, while Area 17 is innervated by X-cells and by Y-cell collaterals from axons terminating in Area 18.

In summary, the data support the termination of X-cells (and some Y-collaterals) in Area 17. Y-cells terminate predominately in Area 18.

In relation to the second criterion, recent evidence suggests that extraretinal, proprioceptive eye position information projects to Area 17. Buisseret and Maffei (1977) have stimulated (after eye removal) the intraorbital part of the motor branches of extraocular muscles where the proprioceptive fibers are located. Recording of visual cells in Area 17 of occipital cortex indicated that 25% of the cells isolated responded to stimulation of another muscle. Since only the lateral rectus, inferior oblique and superior oblique muscles were used in the experiment, the small percentage of activated cortical cells could be misleadingly low due to stimulation of inappropriate muscles. These data then, support the availability of extraretinal eye position information to visual cells located in Area 17 of occipital cortex.

The third criterion, corticofugal innervation of the LGN, is supported by both anatomical (Guillery, 1967;

Hollander, 1970; Gilbert & Kelly, 1975; Updyke, 1975, 1977) and physiological (Widen & Ajmone-Marsan, 1960; Ajmone-Marsan & Morillo, 1961; Vastola, 1960; Kalil & Chase, 1970) data. Various methods for following fibers in the nervous system have been used to understand the corticofugal pathways to the LGN, among them autoradiography and electrophysiology. Each method has indicated that pathways from Area 17 in striate cortex to geniculate exist.

Using autoradiography, Updyke (1975, 1977) has determined that Area 17 projects heavily and uniformly throughout all laminae. Area 18 has similar destinations but is sparse and less uniformly distributed.

Data derived from electrophysiology support the influence of visual cortex on the LGN. Briefly, there are two general methods to determine the extent of cortical input on LGN functioning: (1) inactivation of the visual cortex and determination of geniculate effects, (2) stimulation of occipital cortex while recording LGN units.

The first method has been used by Kalil and Chase (1970), and Vastola (1960). Kalil and Chase (1970) recorded LGN unit responses to photic stimulation before, during, and after reversible cortical cooling. In more than half of the recorded cells there was a statistically significant change in mean frequency of discharge. Vastola (1960) inactivated visual cortex by cathodal polarization. Data indicated the net effect of corticofugal influence was facilitory.

The response of LGN units to stimulation in the visual cortex is the second method to determine the influence of cortex on the geniculate. Widen and Ajmone-Marsan (1960) and Ajmone-Marsan and Murillo (1961) activated LGN neurons either by photic stimulation or electrical stimulation of the optic tract. Electrical stimulation of visual cortex during afferent stimulation was shown to either inhibit or facilitate the LGN response. To date, however, there are no data to support cortical influences directly on LGN X-cells. However, the above data do support cortical influence on LGN cells which most likely include X-cells.

In summary, the results presented meet the three criteria posited: (1) X-cells do appear to project to Area 17, while Y-cells project mainly to Area 18, (2) there is proprioceptive eye position information transmitted to Area 17, (3) Area 17 does influence LGN. Given these results, it seems safe to suggest that one way in which monocular paralysis might selectively affect the LGN X-cell population in animals deprived of vision during the period of paralysis is via a cortically mediated pathway that permits integration of what must be discordant eye position information from the two eyes. The eye position information would be integrated into the processing of visual information. As a result, a signal would be transmitted to the LGN X-cell population initiating their functional atrophy or suppression.

The second pathway proposed to account for oculomotor mediation of cell loss in LGN layers A&C was a complex pathway involving the cerebellum. For this pathway to have been involved in the selective X-cell loss, it too would be required to impact relatively selectively on X-cells. Data in support of this selectivity are less direct than that for the corticogeniculate pathway discussed above. Fukada and Stone (1976) stimulated the medial reticular formation and recorded extracellularly in geniculate. They found that geniculate Y-cells were unaffected by the medial reticular formation stimulation but that LGN X-cells receptive field properties were altered. Since the medial reticular formation has close functional links to oculomotor control networks in the brain stem (Milner, 1970, p. 213), oculomotor input from the brain stem also appears to selectively affect geniculate X-cells.

Layer A_1

As discussed previously, disruption of normal binocular inhibitory interactions appear to be sufficient to account for the loss of LGN X-cells in layer A_1 following either monocular paralysis or binocular eyelid suture. For monocular paralysis, the disruption may occur due to interruption of concordant visual input, while for bilateral eyelid suture the disruption seems to be due to lack of patterned visual input. However, the question as to why the loss is specific to X-cells and to the exclusion of Y-cells remains unanswered. There are, however, data

suggesting that primarily LGN X-cells are susceptible to binocular inhibition.

In a recent study, Fukada and Stone (1976) modulated the maintained firing rate of geniculate cells by presenting visual stimuli to the nondominant eye. After finding the receptive field for the dominant eye, the dominant eye was occluded and the corresponding receptive field for the nondominant eye was stimulated by a radial grating. They found that LGN X-cell resting discharge rate is sensitive to inhibitory binocular interaction, whereas Y-cells are susceptible to a brief period of inhibition followed by a long period of excitation. These results suggest that X-cells are more strongly subject than Y-cells to binocular inhibitory interaction.

In summary, the results of Fukada and Stone (1976) confirm the inference of greater susceptibility of LGN X-cells to binocular inhibition. Disruption of this inhibitory process consequent to disrupted binocular vision following either bilateral eye lid suture or monocular paralysis seems a plausible source for the X-cell loss in geniculate layer A_1.

Artifactual Contamination

It is possible that the apparent loss of long latency (X) cells could be attributed to artifacts unrelated to the visual or motoric alterations which the paralysis

and suture procedures effect. For instance, the results could be attributed to trauma induced as the result of the surgery (either paralysis or lid suturing).

With regards to monocular paralysis, it is possible that during the nerve transection procedure, tissue subserving visual system functioning other than the targeted motor nerves themselves (such as optic nerve or tract) was disturbed, thus in some fashion initiating the observed loss of a cell type. This seems unlikely for several reasons. First, transection surgery was performed under the microscope, permitting visually guided dissection of each nerve as it coursed toward the orbit. The optic chiasm and optic nerve were not disturbed during the surgery. These structures remained intact even to their body coverings, thus limiting the risk of infection or inadvertent mechanical injury. Central visual structures were presumably also unaffected since the meninges remained intact. Second, even if surgical trauma induced by the transection procedure is considered as the basis for the loss observed in the monocular paralysis preparation, it does not explain the similar loss following chronic bilateral eye lid suturing. Presumably, eyelid suturing is not surgically as traumatic as transection of cranial nerves and in lid suture damage to visual structures can virtually be eliminated as a possibility. Thus trauma or inadvertent damage is not a likely explanation for the observed loss following

lid closure. Since a loss of long latency cells was observed following either monocular paralysis or eyelid suture, it seems reasonable to conclude that the surgical preparation per se is not involved.

A further reason for discounting damage to optic structures as the basis for the apparent loss of long latency cells with monocular paralysis is derived from Cook, Walker, and Barr (1951). For damage to the optic nerve or tract to initiate the loss of LGN long latency cells, transneuronal degeneration would have to occur within the fifteen day postsurgical period in which the loss of X-cells occurs. Cook, Walker, and Barr (1951) have found that even following ennucleation or severe optic tract damage, transneuronal degeneration does not occur in less than thirty days.

And finally, if the paralysis surgery per se were responsible for the observed cell loss, it would be expected that the effect would always occur subsequent to monocular paralysis surgery. However, at least in lamina A_1, paralysis surgery combined with bilateral lid suture does not produce a significant X-cell loss. Thus it is safe to conclude that the paralysis surgery per se is not initiating the observed cellular loss.

Other consequences of the surgery per se could, however, have caused the observed results. The surgical intervention used in the paralysis operations does permit

the possibility of inadvertent contact with cranial nerve V, and the venous networks involved in controlling intraocular pressure and venous drainage. Increased intraocular pressure and inadequate venous drainage could have precipitated the geniculate changes by intraocular destruction followed by selected LGN cell transneuronal degeneration. While tonometric assessment was not available, daily inspection of each eye did not reveal obvious corneal scarring or protrusion as would be expected if ocular pressure and venous drainage had been adversely altered by the surgery. Optic disc examination revealed no edema or pallor characteristic of these problems. Furthermore, the changes observed were too rapid to be mediated by a process involving transneuronal degeneration (Cook, Walker, & Barr, 1951).

It is possible, however, that even though increased intraocular pressure and inadequate venous drainage were not evident, some other unknown detrimental effects of the paralysis surgery were in effect. While this seems unlikely, its occurrence still could not account for the apparent loss of long latency cells in (1) the A_1 layer receiving afferents from the unoperated eye, (s) for the losses subsequent to bilateral eyelid suture, or (3) for the reduced losses from monocular paralysis when monocular paralysis is combined with bilateral eyelid suture.

Precaution against the possibility of infection was accomplished via antibiotic maintenance throughout the recovery and recording sessions. It is possible that the antibiotics themselves initiated the loss of the cell population in question. This seems unlikely, however, since these antibiotics have been used extensively in both human and animal clinics, and in the dosages and route of administration used, have never been reported to affect the nervous system as reported here.

Further evidence for excluding disease, drugs or inadvertent damage to optic structures as the causal factors in the observed geniculate change, is provided by the post-recording examination of the experimental brains. In no case was there evidence of infection or trauma.

Another artifact that could account for the significant loss of long latency cells in the experimental preparation concerns the placement of the optic chiasm shock electrode. The stimulating electrode could have been inadvertently placed closer to the LGN in those preparations reported as showing a loss of long latency cells as compared to preparations where no loss was observed. In this case the observed loss would be due to a bias in OX shock electrode placement rather than a physiological anomaly. This seems unlikely since experimental animals show OX latency differences between laminae. These interlaminar differences are absent in the ACMP (normal) animals.

The appearance of the difference in mean OX latency between layers A&C and A_1 in the chronic condition (either monocular paralysis or bilateral lid suture) cannot be accounted for by recourse to bias in shock electrode placement. For any one subject the OX electrode is secured in both the dorso-ventral and anterio-posterior planes. To account for differential mean latency between layers by shock electrode placement would require repeated movement of the shock electrode in the antero-postero direction during each LGN penetration in each recording session rather than systematic bias in the permanent placement of each electrode. This of course is prevented since the shock electrode is secured permanently throughout the experiment.

Yet another way in which the loss of long latency cells could possibly be attributed to circumstances other than a change in geniculate physiology concerns the placement of the recording electrode; that is, the geniculate areas in which the cell recordings were made. It has previously been shown that short and long latency cells are differentially represented in the retina with the central retina containing proportionately more long latency cells and the peripheral retina having a greater representation of short latency cells. It is also known that cells in the lateral geniculate adhere to a retino-topic organization (Bishop, Kozak, Levick, & Vakkur, 1962; Guillery & Kaas, 1971; Sanderson 1971a, b). Thus, there are areas in the

geniculate that contain either proportionately more short latency cells or proportionately more long latency cells. Consequently, if the ACMP subjects were recorded in the geniculate areas representing the central few degrees of visual space (more long latencies) and the CHMP preparations were recorded in the geniculate areas representing the more peripheral regions of retina (more short latencies), a loss of long latency cells would appear to have occurred but it would be due to inappropriate sampling. To insure against this type of error, only cells within the central ten degrees of visual space were analyzed for both the ACMP and CHMP preparation. In the normal cat, this area has an approximately equal representation of short and long latency cells (Hoffman, Stone, & Sherman, 1972).

The loss of long latency cells could also be accounted for by a differential bias in the rate of microelectrode advancement in the experimental and standard (control) preparations. Recent reports indicate that long latency cells have small axons and cell bodies as compared to the short latency cells (Boycott & Wassle, 1971; Stone & Hoffman, 1971, 1972). This fact could make long latency cells more difficult to record. A faster rate of electrode advancement then would differentially decrease the chances of recording longer latency cells due to their small size, while at the same time not relatively increase the chances of

recording the larger, short latency cells. If this occurred, then the observed failure to record long latency cells could be an artifact of the recording procedure. In order to assess this possibility, a comparison of number of cells per pass was made for the experimental and standard groups in each comparison. If the electrode penetrated faster in the experimental groups, one might expect to find fewer cells recorded per pass in the experimental group as compared to the standard or control animals. Correspondingly, if the recording electrode was advanced at the same rate in both groups, one would not find a difference between groups in the number of cells per pass. Number of cells recorded per pass for both the control and experimental groups was, on the average, six cells per pass.

One might question the relative efficiency with which the electrodes used in the present report isolate the short and long latency cells. If electrodes of differing isolation capabilities were used in the experimental and control groups, then the observed loss of long latency cells in the experimental groups could be accounted for on an artifactual basis. This possibility seems unlikely for two reasons. First, electrodes of similar impedance and tip shape were used for both the standard and experimental groups. Further, in many cases, the same electrode was used for both a standard and an experimental

group. Finally, if the electrodes used were not capable of isolating the smaller, long latency cells, then the data recorded for the ACMP preparation would not be similar to previously published data for systemically paralyzed animals.

In summary, there are several artifacts which conceivably could have accounted for the observed cellular loss. However, there appears to be adequate justification for eliminating each source of artifact and concluding rather that the effect is due to the duration of the monocular paralysis or lid suture.

Plasticity Exhibited by Adult and Kitten Visual Systems

The present report indicated that following adult onset monocular paralysis or pattern deprivation a diminished proportion of X-cells remain in the LGN. This is in contrast to the selective loss of LGN Y-cells previously observed following pattern deprivation in kittens. Explanation of the differential X/Y susceptibility to visual system perturbations in adults and kittens, combined with the similarity of some components of the impact of monocular paralysis on the visual system to those in pattern deprivation and strabismus, necessitates a comparison of the effects of monocular paralysis and these other disruptive techniques in adults and kittens.

Until recently, there have been three methods used to alter the visual input of the animal: selective

environmental rearing, pattern deprivation, and disruption of binocular vision without obvious pattern deprivation (strabismus). The effect on visual input produced by selective environmental rearing appears to be unlike that of monocular paralysis and will not be discussed further. There are, however, similarities between monocular paralysis and the other techniques in both adults and kittens.

It should be noted however, that a current attempt at relating the effects of adult onset monocular paralysis to visual deprivation or strabismus in kittens is handicapped. First, the effects of ocular paralysis in the adult and kittens cannot be compared readily since no data on the effects of monocular paralysis in kittens are available.

Second, a comparison between the physiological effects of monocular paralysis and visual deprivation or strabismus, is confounded since the visual distortion imposed upon the organism is different for each disruptive technique. Monocular paralysis achieved through transection of cranial nerves III, IV, and VI is similar to the ocular paresis found in strabismus. In each case the visual input is altered such that the same target is not imaged on corresponding points of the two retinae, and the affected eye is not always focused with respect to the targeted image on the normal eye. However, unlike strabismus, the monocular paralysis procedure also dilates the pupil and prevents accommodation in the paralyzed eye thus

altering the normally balanced light input to the two eyes. In contrast, pattern deprivation prevents target imaging on the retinae, but does not necessarily prevent the yoked alignment of the visual axes of the two eyes (even though one or both eyes have been closed). Further, pattern deprivation due to lid suture does not disrupt lenticular or pupillary responses in the same way as does monocular paralysis. While monocular paralysis dilates the pupil, recent data suggest that the pupil of dark-reared kittens is much smaller than pupils of normal kittens under comparable illumination conditions (Cynader, 1977).

And third, in the data currently available, the types of perturbation, duration of perturbation and animal's age at the onset of the perturbation are confounded. At present the effects of monocular paralysis or pattern deprivation in adult animals has been assessed only after short term paralysis. Whereas, in kittens the effects of pattern deprivation or strabismus have been assessed only after much longer durations. With the above reservations in mind, there are comparisons which may be made.

Comparative Effects of Monocular Paralysis Versus Pattern Deprivation and Strabismus

A comparison between the effects of pattern deprivation and monocular paralysis in the adult organism yields the following. At the level of the LGN, the present report indicates a selective loss of a cell type in both short term pattern deprived (present

report) and short-term monocularly paralyzed (present report; Brown & Salinger, 1975) animals. At the cortical level, pattern deprivation in the adult animal does not appear to be effective in altering normal cortical cell functioning (Hubel & Wiesel, 1970), while monocular paralysis does affect cortical cell functioning by decreasing the number of simple cells driven by both eyes (Buchtel, Berlucci, & Mascetti, 1972; Fiorentini & Maffei, 1974; Maffei & Fiorentini, 1976).

A similar comparison, pattern deprivation versus monocular paralysis but ignoring the problems created by unequal age at perturbation onset and unequal duration factors, suggests that with short-term monocular paralysis in the adult and long-term pattern deprivation in the kitten, there is a loss of binocular cortical cells in both groups (Hubel & Wiesel, 1965a; Buchtel, Berlucci, & Mascetti, 1972). However, in adult monocular paralysis the cells in cortex are equally likely to be responsive to either eye, whereas in monocular deprivation cortical cells respond only to the undeprived eye.

At the LGN level, again disregarding the unequal age of perturbation onset and unequal duration factors, short-term monocular paralysis in the adult and long-term pattern deprivation in the kitten produce a selective albeit different, loss of a cell type (Sherman, Hoffman, & Stone, 1972; Brown & Salinger, 1975). In the kitten,

pattern deprivation during the critical period is followed by a failure to record Y-cells (Sherman, Hoffman, & Stone, 1972; Hoffman & Cynader, 1975); while in the adult, monocular paralysis or pattern deprivation is followed by a failure to record X-cells (Brown & Salinger, 1975; present report).

In comparing the effect of monocular paralysis and surgically induced strabismus, the age of onset of perturbation, duration of perturbation, and type of perturbation factors also cannot be separated since there are no data with regards to (1) the effects of short or long term monocular paralysis on the kitten visual system, and (2) the effects of strabismus on the adult. However, a comparison of the effects of short term monocular paralysis on the adult (Buchtel, Berlucci, & Mascetti, 1972; Fiorentini & Maffei, 1974; Maffei & Fiorentini, 1976) and long term strabismus on the kitten (Hubel & Wiesel, 1965b; Maffei & Bisti, 1976; Yinon, 1976) indicates that at the cortical level both procedures produce a significant loss of binocularity. This is not unexpected since both monocular paralysis and strabismus present discordant visual input to the visual system.

Differential Loss of X- and Y-cells in Kittens and Adults.

Since long term pattern deprivation in kittens is followed by a loss of Y-cells, and subsequent to short term monocular paralysis or pattern deprivation in adults

there is a loss of X-cells, the differential losses observed could be due to the type of perturbation (pattern deprivation versus monocular paralysis), the duration of the perturbation (short term versus long term) or the age of perturbation onset (kitten versus adult). Isolation of the factor or factors involved in these differential X/Y-cell losses awaits the examination of (1) kittens with short term bilateral eye suture, (2) kittens with short and long term monocular paralysis, (3) adults with long term monocular paralysis, and (4) adults with long term bilateral eye lid suture.

By way of summary, the adult visual system seems to manifest a plasticity that in some ways is similar to that of the kitten. This continued plasticity may be advantageous from an evolutionary perspective, as will be discussed subsequently.

Implications of X-Cell Loss for Theories of Neural Development in the Mammaliam Visual System

Connectivity

Currently, two models of connectivity in the visual system offer competing explanations for the processing of visual input. Hubel and Wiesel (1962, 1965a, b) suggest that visual input is processed in a serial or hierarchical manner, with retinal ganglion cells connecting LGN cells that, in turn, connect monosynaptically with simple cells in the visual cortex. Simple cortical cells then connect to complex cortical cells,

which, in turn, feed to hypercomplex cortical cells. Opposing this model is that suggesting that processing from retina to cortex occurs in a parallel manner (Stone, 1972).

The parallel model suggests that there are two systems for information processing in the geniculostriate system, one containing slowly conducting cells (X-cells) and one containing rapidly conducting cells (Y-cells). The axons of retinal ganglion X-cells connect directly to LGN X-cells which in turn are thought to connect monosynaptically with cortical simple cells. Axons of LGN cells receive afferents from Y-cells in the retina and project to cortical complex cells.

The loss of X-cells discussed here would, in conjunction with a report by Fiorentini and Maffei (1974), seem to support the parallel processing model. Following monocular immobilization in adult cats, Fiorentini and Maffei found a drastic reduction in the proportion of binocular simple cells, while the proportion of binocular complex cells remained unchanged. These findings (loss of LGN X-cells coupled with defects in simple cortical X-cells) cannot be explained by the hierarchical model but are not inconsistent with the parallel model. The hierarchical model would, since simple cells connect to complex cells, predict a loss of binocularity in complex

cells. This, of course, was not observed by Fiorentini and Maffei (1974).

The Fiorentini and Maffei (1974) report does not address the processing of information on the geniculostriate system. However, given their results, only the parallel processing model could predict changes which might occur at the geniculate level. If slow conducting cells in the geniculate connect directly with simple cortical cells, and only simple cortical cells show a diminished binocularity following chronic monocular paralysis, then, according to the parallel processing model, any changes that might occur in the geniculate concomitant with cortical changes would occur only in the long latency (X) cell population. The data presented here indicate this expected loss in the longer latency cells and therefore support the parallel processing model.

At the same time, the observed attrition of the LGN X-cell population raises a possibility which has not been addressed by the parallel processing model. Fiorentini and Maffei (1974) observed that a percentage of cortical simple cells continued to be excited by the paralyzed eye after chronic monocular paralysis. Since so few LGN X-cells respond to OX stimulation, it seems unlikely that the remaining cortical simple cells receive input solely from LGN X-cells. This suggests that after

chronic monocular paralysis many simple cortical cells may be driven by LGN Y-cells. This convergence of input between X and Y systems onto simple cortical cells is itself not consistent with the parallel processing model.

Neuronal Ontogeny.

Recent advances in developmental neurobiology have permitted tentative answers to two questions which have been asked by generations of scientists: how is development of the nervous system controlled genetically and to what extent does ontogenetic experience modify the nervous system?

One current approach to the two questions is the theory of Functional Validation suggested by Jacobson (1974). In this speculative theory there are two modes of neuronal ontogeny. One group of neurons expresses their function in innate, predetermined ways and a second group is developed from a cell population in which all possible contingencies of function are present.

Jacobson has labeled the two types of cells Class I and Class II neurons. Class I neurons have structure and function which are genetically determined and not subject to change. Class II neurons are susceptible to such factors as availability of space, level of nutrients or hormones and other environmental factors such as sensory stimulation. Further, Class II neurons have multiple functional potentials which are progressively restricted during development. Once the restriction of functional

potential occurs, the neuron is considered "unipotential and functionally unmodifiable."

Class II neurons are also differentiated from Class I neurons on the basis of their position in the afferent-efferent loop. Class I neurons are "large neurons with long axons that form the primary afferent and efferent systems."

Jacobson sees the method of differentiation for Class II neurons as similar to the process of survival of the fittest individuals. That is, Class II neurons exist in such plenitude that every conceivable functional contingency exists and from this diversity "certain neurons are selected for survival on the basis of their response to extrinsic factors such as sensory stimulation or hormonal stimulation" (1974, p. 154). Environmental stimulation, either due to fluctuations in cellular milieu or sensory input, functions in a 'permissive' manner such that it constitutes a "functional validation of the preexisting neuronal structures" (1974, p. 154). Nonvalidated structures cease to exist being reabsorbed or converted to validated structures. The completion of this process in a particular system constitutes the end of that critical period.

Functional validation may explain the plasticity of orientation selectivity of short axon cortical cells in the kitten. Since (1) any particular cell in immature

visual cortex initially responds to a wide variety of orientations, i.e., broadly tuned (Barlow & Pettigrew, 1971; Buisseret & Imbert, 1975), (2) following selective exposure, cells recorded in immature cortex seem to respond only to the previously presented orientation (Blakemore & Cooper, 1970; Hirsch & Spinelli, 1970, 1971), and (3) there are no silent areas in a selectively exposed cortex which would indicate dysfunctional cells (Blakemore & Cooper, 1970), it appears functional validation of pre-existing connections may explain orientation specificity.

However, functional validation fails to account for (1) loss of binocularity in short axon cortical cells (presumably Class I cells) following monocular paralysis in adult cats (Buchtel, Berlucci, & Mascetti, 1972; Fiorentini & Maffei, 1974), (2) the loss of long axon LGN X-cells (presumably Class I cells) following monocular paralysis (Brown & Salinger, 1975; present study) or binocular eye lid suture (present study) in adult cats, or (3) loss of long axon LGN Y-cells (presumably Class I cells) following pattern deprivation in kittens.

That changes occur in short axon cortical cells in adult cats suggests that Class II neurons have the potential for change even after the period of functional validation following which they could reasonably be considered to have become unipotential and functionally unmodifiable. That changes can occur in long axon cells

suggests that differentiation of function is not restricted to short axons cells. That changes in function occur in long axon cells of adults suggests that function of Class I cells is plastic. Taken together, these results seem to indicate that functional validation with its conceptual basis in the critical period does not appear adequate. What may be necessary for functioning of both Class I and some Class II cells is a process whereby they receive proper stimulation on a continuing basis, that is, 'recurrent validation.'

Adult Plasticity--Adaptive Value

Plasticity of the adult nervous system has only been detected using physiological techniques in the last few years. That the nervous system is capable of functional changes after environmental alterations corresponds nicely with current theories of evolution which contend that organisms capable of phenotypic adaptation to their particular ecological niche are the most likely to survive. However, the question arises as to whether the effects observed following perturbations of the visual system are in fact adaptive or merely a response of the nervous system to injury without regard to its adaptive value.

In kittens, modification of orientation specificity may be seen as the 'fine tuning' of the visual system such that it is most responsive to the environment in which it exists. In contrast, the kitten visual system response to

monocular pattern deprivation seems a response to injury without any apparent regard to its adaptive value. Following monocular deprivation, cortical cells are driveable only by the initially open eye (Wiesel & Hubel, 1963b) and there is a functional loss of LGN Y-cells (Sherman, Hoffman & Stone, 1972; Hoffman & Cynader, 1975). On the surface, loss of a cell type and loss of binocularity appear not to be adaptive.

In the adult cat, monocular paralysis causes a loss of binocularity of simple cells in cortex as well as a functional loss of LGN X-cells. The same appears to be true of binocular pattern deprivation in adults with respect to loss of LGN X-cells. Again, at first inspection, these changes would appear to be a nervous system response to major injury without apparent regard to adaptive value. The loss of LGN X-cells during bilateral eye lid suture would seem to be the response of the visual system to injury without regard to adaptive value in the sense that it is hard to imagine a visual system adaptation to blindness. However, there is a possibility that the losses following monocular paralysis serve to eliminate systemic noise that might disrupt the remaining capacity of the visual system after injury.

Monocular paralysis causes strabismus, a misalignment of the visual axes of the two eyes, with each eye viewing a different target in space. This would suggest

that two radically different images need to be processed simultaneously by the visual system, a task for which the visual system probably is not prepared. In order to permit adequate vision, only one of the abnormally disparate images may be processed at any instant in time. In order to minimize disruption while maintaining vision, the visual system might eliminate some visual processing from one eye. This is known as 'suppression' and would produce amblyopia. In this fashion, some visual capability free of diplopia could be maintained.

Manifestations of Adult Plasticity in Animals--Parallels in Human Visual Dysfunction

The present experiments demonstrate visual system plasticity in adult animals. That the visual system in animals has the capacity for change subsequent to a sensitive developmental period suggests the possibility that syndromes seen in human ophthalmology, whose residues have not been considered amenable to treatment since they were produced during the critical period, might be treatable in adult patients. One such syndrome, decreased visual acuity in the presence of normal optics (amblyopia), can be initiated by youthful cataracts or squint and is seen often in clinical practice (von Noorden, 1973, 1974).

The effects on visual system functioning attendant to cataracts and squint in humans appears to be analogous to the effects of bilateral lid suture and monocular

paralysis as used in the present report with animals. However, there is difficulty in comparing the results of studies with animal subjects and those involving human patients.

First, many animal studies are restricted to results from neurophysiological methods. This is true of the present report wherein single unit electrophysiology was used to ascertain the consequences of eye paralysis and lid suture. In the human patient such data are unattainable.

Second, the present work is concerned with adult visual system perturbations. Until recently treatment of adult amblyopia arising out of childhood strabismus has not been considered advantageous and consequently there is a scarcity in the human literature concerning treatment of adults.

And third, although there are data available on the effects of monocular patching in adult animals and humans, and binocular patching in adult and immature animals, there are none available for binocular patching in adult and immature humans. With these limitations in mind, the following comparisons may be made.

Pattern Deprivation

The immediate effect of lid suture in either adult or immature subjects is prevention of pattern vision. In the human patient, pattern deprivation occurs naturally as a consequence of corneal opacities or

congenital cataracts, as well as patching for corneal abrasions and injury to globe.

Following monocular lid suture initiated during the first few weeks after birth, several studies have found that both cats and monkeys appear blind when forced to use the deprived eye (Dews & Wiesel, 1970; Baker, Grigg, & von Noorden, 1974; Movshon, 1976b; Hendrickson, Boles, & McLean, 1977). Tests of acuity have indicated these experimental animals are amblyopic (von Noorden, Dowling, & Ferguson, 1970; von Noorden, 1973; Baker, Grigg, & von Noorden, 1974). Also, following pattern deprivation, the young human patient experiences diminished acuity in the affected eye (Burian, 1966; Frey, Friendly, & Wyatt, 1973; von Noorden, 1974, 1976). Thus, there seems to exist a parallel between deprivation effects in animals and some aspects of the clinical picture in humans.

Misalignment of Visual Axes

A parallel between effects of monocular paralysis and strabismus in animals, and strabismus in humans, may also exist. One immediate result of monocular paralysis (along with pupil dilation and accommodation dysfunction) is to prevent convergence of the two eyes. Inability to control convergence of the two eyes is also experienced by human strabismics.

Strabismus in animals yields amblyopia. Von Noorden et al. (von Noorden, 1973; von Noorden & Dowling, 1970; von Noorden, Dowling, & Ferguson, 1970; Baker, Grigg, & von

Noorden, 1974) induced esotropia in monkeys. Without exception they found animals that were extremely amblyopic. In parallel to those findings in animals, strabismic patients who are suppressors and use only one eye effectively have an acuity loss in the suppressed eye.

X-Cells and Amblyopia

Lid suture and strabismus each prevent focused pattern input to the affected eye. In the case of lid suture, pattern vision is prevented. Whereas, for strabismics the pattern is degraded since it is out of focus. Recently, Ikeda and Wright (1974) have suggested that amblyopia following early induction of strabismus is due to inappropriate stimulation of the X pathway during development. They base this hypothesis on the results of several experiments indicating that X-cells are most likely responsible for acuity functions. Retinal X-cells have higher grating acuity and they progressively cease responding much more rapidly than Y-cells as an image is defocused (Ikeda & Wright, 1972, 1976a). These characteristics suggest that X-cells could serve as the physiological substrate of acuity functions.

If retinal X-cells are responsible for acuity functions and induced squint in animals initiates amblyopia in the deviating eye, then geniculate cells in animals with squint may be altered in those layers innervated by the deviating eye, and essentially unaltered in the layers innervated by the dominant eye. This hypothesis was tested

by Ikeda and Wright (1976a, b) using kittens reared with convergent squint. Using spatial resolution threshold, they determined the visual acuity of LGN X-cells in those layers innervated by the dominant and deviating eye respectively. LGN X-cells receiving input from the squint eye had reduced peak firing frequencies and reduced response to higher spatial frequencies when compared to X-cells innervated by the dominant eye. These findings are consistent with the hypothesis suggesting that X-cells are more susceptible to squint than Y-cells.

The data suggesting that functioning of X-cells is disrupted by defocusing seem to be consistent with the diminished proportion of X-cells recorded in the LGN layers A&C following monocular paralysis and layer A_1 following adult onset bilateral eye lid suture. However, it does not explain the loss of X-cells in layers A&C following monocular paralysis since Experiment III indicated that the A&C layers are disrupted not by retinally mediated factors but rather extra-retinally mediated factors. Further, it does not explain the loss of LGN X-cells in the layer innervated by the mobile, unoperated eye in the monocular paralysis preparation since the X-cells are innervated by the normal eye.

Adult Plasticity--Implications for Clinical Ophthalmology

To the extent that studies using animals discussed in the previous section generate data that parallel findings in the human visual system, then treatment regimens based upon animal data seem feasible. As such, the existence of visual system plasticity in adult amblyopia due to early onset strabismus may be successfully treated. Data in human literature seem to support this assumption.

Until recently, treatment for amblyopia was limited to those patients in whom the syndrome was detected early. Ophthalmologists concluded that the visual system was not subject to modification past age six and therefore considered treatment to be useless past that age (Frey, Friendly, & Wyatt, 1973). However, there are conflicting reports on the capability of older amblyopics to benefit from intensive ocular therapy. Several clinicians have reported success in treating amblyopia of various etiologies in patients afflicted during early life but treated as older children or adolescents (von Noorden, 1965; Callahan & Berry, 1968; von Noorden, Springer, Romono, & Parks, 1970; Gould, Fishkoff, & Galin, 1970; Nawratztki, 1976). Each of these studies has in common the forced usage of the amblyopic eye after patching the dominant eye. Forced usage does not merely mean exposure of the deviating eye to normal visual input but rather the patient uses the eye to perform various tasks. For example,

Gould, Fishkoff and Galin (1970) found that children older than ten years benefit from circling specific letters in newspapers placed at varying distances from the patient. With the dominant eye patched, the patient begins circling letters with the newspaper relatively close and then as his acuity improves the newspaper is moved farther from the eye. Von Noorden et al. (von Noorden, Spring, Romono, & Parks, 1970) found similar results using patients as old as sixteen years. These patients colored different symbols of decreasing size in an exercise book. Again, the dominant eye was patched during a 1/2 hour daily exercise period.

These successful treatments for older amblyopics is consistent with the data presented in this paper indicating the existence of an extended period of visual system plasticity. The key to treatment success in human amblyopes seems to be exercise of the affected eye.

REFERENCES

Ajmone-Marsan, C., & Morillo, A. Cortical control and callosal mechanisms in the visual system of cat. Electroencephalography and Clinical Neurophysiology, 1961, 13, 553-563.

Bach-y-Rita, P., & Ito, P. Properties of stretch receptors in cat extraocular muscles. Journal of Physiology, 1966, 186, 663-688.

Baker, F. H., Grigg, P., & von Noorden, G. K. Effects of visual deprivation and strabismus on the response of neurones in the visual cortex of the monkey, including studies on the striate and prestriate cortex in the normal animal. Brain Research, 1974, 66, 185-208.

Baker, R., Precht, W., & Llinas, R. Mossy and climbing fiber projections of extraocular muscle afferents to the cerebellum. Brain Research, 1972, 38, 440-445.

Barlow, H. G., & Pettigrew, J. D. Lack of specificity of neurones in the visual cortex of young kittens. Journal of Physiology, 1971, 218, 98-990.

Batini, C., Buisseret, P., & Kado, R. T. Extraocular proprioceptive and trigeminal projections to the Purkinje cells of the cerebellar cortex. Archives Italliennes de Biologie, 1974, 112, 1974.

Berman, N., & Daw, N. W. Comparison of the critical periods for monocular and directional deprivation in cats. Journal of Physiology, 1977, 265, 249-259.

Bishop, P. O., Burke, W., & Davis, R. The interpretation of the extracellular response of single lateral geniculate cells. Journal of Physiology, 1962, 162, 451-472.

Bishop, P. O., Kozak, W., Levick, W. R., & Vakkur, G. J. The determination of the projection of the visual field on to the lateral geniculate nucleus in the cat. Journal of Physiology, 1962, 163, 503-539.

Blake, R., Crawford, M. L. J., & Hirsch, H. V. B. Consequences of alternating monocular deprivation on eye alignment and convergence in cats. Investigative Ophthalmology, 1974, 13, 121-125.

Blakemore, C. Developmental factors in the formation of feature extracting neurons. In F. O. Schmitt & F. G. Worden, The Neurosciences Third Study Program. Cambridge, Mass.: MIT Press, 1974. Pp. 105-113.

Blakemore, C., & Cooper, G. F. Development of the brain depends on the visual environment. Nature (London), 1970, 228, 477-478.

Blakemore, C., & van Sluyters, R. C. Reversal of the physiological effects of monocular deprivation in kittens: Further evidence for a sensitive period. Journal of Physiology, 1974, 237, 195-216.

Blakemore, C., & van Sluyters, R. C. Innate and environmental factors in the development of the kitten's visual cortex. Journal of Physiology, 1975, 248, 663-716.

Blakemore, C., van Sluyters, R. C., Peck, C., & Hein, A. Development of cat visual cortex following rotation of one eye. Nature (London), 1975, 257, 584-586.

Boycott, B. B., & Wassle, H. The morphological types of ganglion cells of the domestic cat's retina. Journal of Physiology, 1974, 240, 397-419.

Brown, D. L., & Salinger, W. L. Loss of X-cells in lateral geniculate nucleus with monocular paralysis: Neural plasticity in the adult cat. Science, 1975, 189, 1011-1012.

Buchtel, H. A., Berlucci, G., & Mascetti, G. G. Modifications in visual perception and learning following immobilization of one eye in cats. Brain Research, 1972, 37, 355-356.

Buisseret, P., & Imbert, M. Responses of neurones in the striate cortex observed in normal and dark-reared kittens during post-natal life. Journal of Physiology, 1975, 246, 98-99P.

Buisseret, P., & Maffei, L. Extraocular proprioceptive projections to the visual cortex. Experimental Brain Research, 1977, 28, 421-425.

Burian, H. M. Occlusion amblyopia and the development of eccentric fixation in occluded eyes. American Journal of Ophthalmology, 1966, 62, 853-856.

Callahan, W. P., & Berry, D. The value of visual stimulation during constant and direct occlusion. American Orthoptic Journal, 1968, 18, 73-74.

Cleland, B. G., & Levick, W. R. Physiology of cat retinal ganglion cells. Investigative Ophthalmology, 1972, 11, 285-291.

Cleland, B. G., & Levick, W. R. Brisk and sluggish concentrically organized ganglion cells in the cat's retina. Journal of Physiology, 1974, 240, 421-456.

Cleland, B. D., Dubin, M. W., & Levick, W. R. Sustained and transient neurones in the cat's retina and lateral geniculate nucleus. Journal of Physiology, 1971, 217, 473-496.

Cleland, B. G., Levick, W. R., & Sanderson, K. J. Properties of sustained and transient ganglion cells in the cat retina. Journal of Physiology, 1973, 228, 649-680.

Cleland, B. G., Levick, W. R., & Wassle, H. Physiological identification of a morphological class of cat retinal ganglion cells. Journal of Physiology, 1975, 248, 151-171.

Cook, W. H., Walker, J. H., & Barr, M. L. A cytological study of transneuronal atrophy in the cat and rabbit. Journal of Comparative Neurology, 1951, 94, 267-291.

Cynader, M. The etiology of strabismus in the cat. Paper presented at Association for Research in Vision and Ophthalmology Annual Meeting, 1977.

Cynader, M., & Chernenko, G. Abolition of direction selectivity in the visual cortex of the cat. Science, 1976, 193, 504-505.

Cynader, M., Berman, N., & Hein, A. Cats reared in stroboscopic illumination: Effects on receptive fields in visual cortex. Proceedings of the National Academy of Sciences, USA, 1973, 70, 1353-1354.

Daw, N. W., & Wyatt, H. J. Kittens reared in a unidirectional environment: Evidence for a critical period. Journal of Physiology, 1976, 257, 155-170.

Dews, P. B., & Wiesel, T. N. Consequences of monocular deprivation on visual behavior in kittens. Journal of Physiology, 1970, 206, 437-455.

Dreher, B., & Sanderson, K. J. Receptive field analysis: Responses to moving visual contours by single lateral geniculate neurons. Journal of Physiology, 1973, 234, 95-118.

Dursteler, M. R., Garey, L. J., & Movshon, J. A. Reversal of the morphological effects of monocular deprivation in the kitten's lateral geniculate nucleus. Journal of Physiology, 1976, 261, 189-210.

Enroth-Cugell, C., & Robson, J. G. The contrast sensitivity of retinal ganglion cells of the cat. Journal of Physiology, 1966, 187, 517-552.

Fernald, R., & Chase, R. An improved method for plotting retinal landmarks and focusing the eyes. Vision Research, 1971, 11, 95-96.

Fiorentini, A., & Maffei, L. Change of binocular properties of the simple cells of the cortex in adult cats following immobilization of one eye. Vision Research, 1974, 14, 217-218.

Frey, T., Friendly, P., & Wyatt, D. Re-evaluation of monocular cataracts in children. American Journal of Orthoptics, 1973, 76, 381-388.

Fuchs, A. L., & Kornhuber, H. H. Extraocular muscle afferents to the cerebellum of the cat. Journal of Physiology, 1969, 200, 713-722.

Fukada, Y. Receptive field organization of cat optic nerve fibers with special reference to conduction velocity. Vision Research, 1971, 11, 209-226.

Fukada, Y. Differentiation of principal cells of the cat lateral geniculate body into two groups: fast and slow cells. Experimental Brain Research, 1973, 17, 242-260.

Fukada, Y., & Saito, H. Phasic and tonic cells in the cat's lateral geniculate nucleus. Tohoku Journal of Experimental Medicine, 1972, 106, 209-210.

Fukada, Y., & Stone, J. Retinal distribution and central projections of Y-, X-, and W-cells of the cat's retina. Journal of Neurophysiology, 1974, 37, 749-772.

Fukada, Y., & Stone, J. Evidence of differential influences on X- and Y-type relay cells in the cat's lateral geniculate nucleus. Brain Research, 1976, 112, 188-196.

Garey, L. J., & Blakemore, C. The effects of monocular deprivation on different neuronal classes in the lateral geniculate nucleus of the cat. Experimental Brain Research, 1977, 28, 259-278.

Garey, L. J., & Powell, T. P. S. The projection of the lateral geniculate nucleus upon the cortex of the cat. Proceedings of the Royal Society of London, 1967, 169, 107-126.

Gilbert, C. D., & Kelly, J. P. The projections of cells in different layers of the cat visual cortex. Journal of Comparative Neurology, 1975, 163, 81-106.

Gould, A., Fishkoff, D., & Galin, M. A. Active visual stimulation: A method of treatment of amblyopia in older patients. American Orthopic Journal, 1970, 20, 39-45.

Guillery, R. W. A study of golgi preparations from the dorsal lateral geniculate nucleus of the adult cat. Journal of Comparative Neurology, 1966, 128, 21-49.

Guillery, R. W. Patterns of fiber degeneration in the dorsal lateral geniculate nucleus of the cat following lesions in the visual cortex. Journal of Comparative Neurology, 1967, 130, 197-213.

Guillery, R. W. The laminar distribution of retinal fibers in dorsal lateral geniculate nucleus of the cat: A new interpretation. Journal of Comparative Neurology, 1970, 138, 339-368.

Guillery, R. W., & Kaas, J. H. A study of normal and congenitally abnormal retino-geniculate projections in cats. Journal of Comparative Neurology, 1971, 143, 73-100.

Hayhow, W. R. The cytoarchitecture of the lateral geniculate body in the cat in relation to the distribution of crossed and uncrossed optic fibers. Journal of Comparative Neurology, 1958, 110, 1-64.

Hendrickson, A., Boles, J., & McLean, E. B. Visual acuity and behavior of monocularly deprived monkeys after retinal lesions. Investigative Ophthalmology and Visual Science, 1977, 16, 469-473.

Hickey, T. L., & Guillery, R. W. An autoradiographic study of retinogeniculate pathways in the cat and fox. Journal of Comparative Neurology, 1974, 156, 239-254.

Hirsch, H. V. B., & Spinelli, D. N. Visual experience modifies distribution of horizontally and vertically oriented receptive fields in cats. Science, 1970, 168, 869-871.

Hirsch, H. V. B., & Spinelli, D. N. Modification of the distribution of receptive field orientation in cats by selective visual exposure during development. Experimental Brain Research, 1971, 13, 509-527.

Hoffman, K-P., & Cynader, M. Recovery in the LGN of the cat after early deprivation. Brain Research, 1975, 85, 179.

Hoffman, K-P., Stone, J., & Sherman, S. M. Relay of receptive-field properties in dorsal lateral geniculate nucleus of the cat. Journal of Neurophysiology, 1972, 35, 518-531.

Hollander, H. The projection from the visual cortex to the lateral geniculate body (LGB). An experimental study with silver impregnation methods in the cat. Experimental Brain Research, 1970, 10, 219-235.

Hollander, H., & Vanegas, H. The projection from the lateral geniculate nucleus onto the visual cortex in the cat. A quantitative study with horseradish-peroxidase. Journal of Comparative Neurology, 1977, 173, 519-536.

Hubel, D. H. Single unit activity in lateral geniculate body and optic tract of unrestrained cats. Journal of Physiology, 1960, 150, 91-104.

Hubel, D. H., & Wiesel, T. N. Receptive fields of single neurones in the cat's striate cortex. Journal of Physiology, 1959, 148, 574-591.

Hubel, D. H., & Wiesel, T. N. Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. Journal of Physiology, 1962, 160, 106-154.

Hubel, D. H., & Wiesel, T. N. Receptive fields and functional architecture in two non-stirate visual areas (18 and 19) of the cat. Journal of Neurophysiology, 1965a, 28, 229-289.

Hubel, D. H., & Wiesel, T. N. Binocular interaction in striate cortex of kittens reared with artificial squint. Journal of Neurophysiology, 1965b, 28, 1041-1059.

Hubel, D. H., & Wiesel, T. N. The period of susceptibility to the physiological effects of unilateral eye closure in kittens. Journal of Physiology, 1970, 206, 419-436.

Ikeda, H., & Wright, M. J. Differential effects of refractive errors and receptive field organization of central and peripheral ganglion cells. Vision Research, 1972, 12, 1465-1476.

Ikeda, H., & Wright, M. J. Is amblyopia due to inappropriate stimulation of the sustained pathway during development? British Journal of Ophthalmology, 1974, 58, 165-175.

Ikeda, H., & Wright, M. J. Retinotopic distribution, visual latency, and orientation tuning of 'sustained' and 'transient' cortical neurones in area 17 of the cat. Experimental Brain Research, 1975, 22, 385-398.

Ikeda, H., & Wright, M. Neurophysiological basis of squint amblyopia. Spatial resolution of Neurones in the lateral geniculate nucleus of kittens reared with convergent squint in one eye. In S. Moore, J. Mein, & L. Stockbridge, Orthoptics, past, present, future. New York: Straton Intercontinental Medical Book Corporation, 1976.

Ikeda, H., & Wright, M. J. Properties of LGN cells in kittens reared with convergent squint: A neurophysiological demonstration of amblyopia. Experimental Brain Research, 1976, 25, 63-77.

Jacobson, M. Developmental neurobiology. New York: Holt, 1970.

Jacobson, M. A plentitude of neurons. In G. Gottlieb (Ed.), Studies on the development of behavior and the nervous system. New York: Academic Press, 1974.

Jeannerod, M., & Putkonen, P. T. S. Oculomotor influences on the lateral geniculate body neurons. Brain Research, 1970, 24, 125-129.

Jeannerod, M., & Putkonen, P. T. S. Lateral geniculate unit activity and eye movements: Saccade-locked changes in dark and in light. Experimental Brain Research, 1971, 13, 533-546.

Jeannerod, M., & Sakai, K. Occipital and geniculate potentials related to eye movements in the unanaesthetized cat. Brain Research, 1970, 19, 361-377.

Kaas, J. H., Guillery, R. W., & Allman, J. M. Some principles of organization in the dorsal lateral geniculate nucleus. Brain, Behavior, and Evolution, 1972, 6, 253-299.

Kalil, R. E., & Chase, R. Corticofugal influence on activity of lateral geniculate neurons in the cat. Journal of Neurophysiology, 1970, 33, 459-474.

Kupfer, C., & Palmer, P. Lateral geniculate nucleus: Histological and cytochemical changes following afferent denervation and visual deprivation. Experimental Neurology, 1964, 9, 400-409.

Maffei, L., & Bisti, S. Binocular interaction in strabismic kittens deprived of vision. Science, 1976, 191, 579-580.

Maffei, L., & Fiorentini, A. Asymmetry of motility of the eyes and change of binocular properties of cortical cells in adult cats. Brain Research, 1976, 105, 73-78.

Milner, P. M. Physiological psychology. New York: Holt, Rinehart, & Winston, Inc., 1970.

Movshon, J. A. Reversal of the physiological effects of monocular deprivation in the kitten's visual cortex. Journal of Physiology, 1976a, 261, 125-174.

Movshon, J. A. Reversal of the behavioural effects of monocular deprivation in kittens. Journal of Physiology, 1976b, 261, 175-188.

Nawratzki, I. Changing approaches to the treatment of amblyopia. In S. Moore, J. Mein, & L. Stockbridge, Orthoptics, past, present, future. New York: Stratton Intercontinental Medical Book Corporation, 1976, 93-98.

Noda, H., & Adey, W. R. Excitability changes in cat lateral geniculate cells during saccadic eye movements. Science, 1974, 183, 543-545.

Olson, C. R., & Pettigrew, J. C. Single units in visual cortes of kittens reared in stroboscopic illumination. Brain Research, 1974, 70, 189-204

Orem, J., Schlag-Ray, M., & Schlag, J. Unilateral visual neglect and thalamic intralaminar lesions in the cat. Experimental Neurology, 1973, 40, 784-797.

Peck, C. K., & Blakemore, C. Modification of single neurons in the kitten's visual cortex after brief periods of monocular visual experience. Experimental Brain Research, 1975, 22, 57-68.

Pettigrew, J. D., & Freeman, R. D. Visual experience without lines: Effect on developing cortical neurons. Science, 1973, 182, 599-601.

Pettigrew, J. D., & Garey, L. J. Selective modification of single neuron properties in the visual cortex of kittens. Brain Research, 1974, 66, 160-164.

Pettigrew, J. D., Olson, C., & Barlow, H. B. Kitten visual cortex: short-term stimulus induced changes in connectivity. Science, 1973, 180, 1202-1203.

Pettigrew, J. D., Olson, C., & Hirsch, H. V. B. Cortical effects of selective visual experience: degeneration or reorganization. Brain Research, 1973, 51, 345-351.

Salinger, W. L., Ward, S., & Hooker, L. Volume changes in lateral geniculate nucleus of adult cats after brief periods of monocular paralysis. Paper presented at Association for Research in Vision and Ophthalmology Annual Meeting, Sarasota, Fla., 1977

Sanderson, K. J. The projection of the visual field in the lateral geniculate and medial interlaminar nucleus in the cat. Journal of Comparative Neurology, 1971, 143, 101-118.

Sanderson, K. F. Visual field projection columns and magnification factors in the lateral geniculate nucleus of the cat. Experimental Brain Research, 1971, 13, 159-177.

Sanderson, K. J., Bishop, P. O., & Darian-Smith, I. The properties of the binocular receptive fields of lateral geniculate neurons. Experimental Brain Research, 1971, 13, 179-207.

Schmielau, F., & Singer, W. The role of visual cortex for binocular interaction in the cat lateral geniculate nucleus. Brain Research, 1977, 120, 354-361.

Sherman, S. M., & Stone, J. Physiological normality of the retina in visually deprived cats. Brain Research, 1973, 60, 224-230.

Sherman, S. M., & Sanderson, K. J. Binocular interaction on cells of the dorsal lateral geniculate nucleus of visually deprived cats. Brain Research, 1972, 37, 126-131.

Sherman, S. M., Hoffman, K-P., & Stone, J. Loss of a specified cell type from geniculate nucleus in visually deprived cats. Journal of Neurophysiology, 1972, 35, 532-541.

Shinkman, P. G., & Bruce, C. J. Binocular differences in cortical receptive fields of kittens after rotationally disparate binocular experience. Science, 1977, 197, 285-287.

Schlaer, R. Shift in binocular disparity causes compensatory change in the cortical structure of kittens. Science, 1971, 173, 638-641.

Siegel, S. Nonparametric statistics for the behavioral sciences. New York: McGraw-Hill, 1956.

Singer, W. Inhibitory binocular interaction in the lateral geniculate body of the cat. Brain Research, 1970, 18, 165-170.

Snider, R. S., & Niemer, W. T. A stereotaxic atlas of the cat brain. Chicago: University of Chicago Press, 1961.

Stone, J. Morphology and physiology of the geniculocortical synapse in the cat: The question of parallel input to the striate cortex. Investigative Ophthalmology, 1972, 11, 338-346.

Stone, J., & Dreher, B. Projection of X- and Y-cells of the cat's lateral geniculate nucleus to Areas 17 and 18 of visual cortex. Journal of Neurophysiology, 1973, 36, 551-567.

Stone, J., & Hoffman, K-P. Conduction velocity as a parameter in the organization of the afferent relay in the cat's lateral geniculate nucleus. Brain Research, 1971, 32, 454-459.

Stone, J., & Hoffman, K-P. Very slow-conducting ganglion cells in the cat's retina: A major, new functional type? Brain Research, 1972, 43, 610-616.

Suzuki, H., Kato, E. Binocular interaction at cat's lateral geniculate body. Journal of Neurophysiology, 1966, 29, 909-920.

Suzuki, H., & Takahashi, M. Organization of lateral geniculate neurones in binocular inhibition. Brain Research, 1970, 23, 261-264.

Tretter, F., Cynader, M., & Singer, W. Cat parastriate cortex: A primary or secondary visual area. Journal of Neurophysiology, 1975, 38, 1099-1113.

Updyke, B. V. The patterns of projection of cortical areas 17, 18 and 19 onto the laminae of the dorsal lateral geniculate nucleus of the cat. Journal of Comparative Neurology, 1975, 163, 377-396.

Updyke, B. V. Topographic organization of the projections from cortical areas 17, 18, and 19 onto the thalamus, pretectum and superior colliculus in the cat. Journal of Comparative Neurology, 1977, 173, 81-121.

Vastola, E. F. Binocular inhibition in the lateral geniculate body. Experimental Neurology, 1960, 2, 221-231.

Von Noorden, G. K. Occlusion therapy in amblyopia with eccentric fixation. Archives of Ophthalmology, 1965, 73, 776-781.

Von Noorden, G. K. Experimental amblyopia in monkeys. Further behavioral observations and clinical correlations. Investigative Ophthalmology, 1973, 12, 721-726.

Von Noorden, G. K. Factors involved in the production of amblyopia. British Journal of Ophthalmology, 1974, 58, 158-164.

Von Noorden, G. K. Current concepts of amblyopia. In S. Moore, J. Mein, & L. Stockbridge, Orthoptics, past, present, and future. New York: Stratton Intercontinental Medical Book Corporation, 1976.

Von Noorden, G. K., & Dowling, J. E. Experimental amblyopia in monkeys. II. Behavioral studies in strabismic amblyopia. Archives of Ophthalmology, 1970, 84, 215-220.

Von Noorden, G. K., Dowling, J. E., & Ferguson, D. C. Experimental amblyopia in monkeys. I. Behavioral studies of stimulus deprivation amblyopia. Archives of Ophthalmology, 1970, 84, 206-214.

Von Noorden, G. K., Springer, F., Romano, P., & Parks, M. Home therapy for amblyopia. American Orthoptic Journal, 1970, 20, 46-50.

Widen, L., & Ajmone-Marsan, C. Effects of corticopetal and corticofugal impulses upon single elements of the dorsal lateral geniculate nucleus. Experimental Neurology, 1960, 2, 468-502.

Wiesel, T. N., & Hubel, D. H. Effects of visual deprivation on morphology and physiology of cells in the cat's lateral geniculate body. Journal of Neurophysiology, 1963a, 26, 978-993.

Wiesel, T. N., & Hubel, D. H. Single-cell responses in striate cortex of kittens deprived of vision in one eye. Journal of Neurophysiology, 1963b, 26, 1003-1017.

Wiesel, T. N., & Hubel, D. H. Comparison of the effects of unilateral and bilateral eye closure on cortical unit responses in kittens. Journal of Neurophysiology, 1965a, 28, 1029-1040.

Wiesel, T. N., & Hubel, D. H. Extent of recovery from the effects of visual deprivation in kittens. Journal of Neurophysiology, 1965b, 28, 1060-1072.

Yinon, U. Age dependence of the effect of squint on cells in kittens' visual cortex. Experimental Brain Research, 1976, 26, 151-157.

APPENDIX: OX Latency Distributions for Individual Cats

Table A

Distributions of OX Latencies Recorded in the A&C Layers of the Right Geniculate in ACMP Animals

Cat 133		Cat 142		Cat 149		Cat 152	
Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)
2.7	100	1.0	6.8	1.2	33.3	1.0	14.3
		1.2	22.7	1.5	33.3	1.1	21.4
		1.3	4.5	2.1	33.3	1.2	7.1
		1.4	2.3			1.7	7.1
		1.5	4.5			1.8	7.1
		1.6	4.5			1.9	7.1
		1.7	4.5			2.0	14.3
		1.8	2.3			2.5	14.3
		1.9	4.5			2.7	7.1
		2.0	2.3				
		2.1	9.1				
		2.2	4.5				
		2.3	15.9				
		2.6	2.3				
		2.7	4.5				
		2.8	4.5				

Table B

Distributions of OX Latencies Recorded in the A_1 Layer of the Right Geniculate in ACMP Animals

Cat 133		Cat 142		Cat 149		Cat 152	
Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)
1.6	7.7	0.8	16.7	1.1	4.1	1.3	20.0
1.8	15.4	1.2	8.3	1.3	4.1	1.5	40.0
1.9	23.1	1.5	8.3	1.4	4.1	1.8	40.0
2.0	7.7	1.6	8.3	1.6	33.3		
2.1	7.7	1.7	41.7	2.0	11.1		
2.2	23.1	2.0	8.3	2.4	11.1		
2.3	7.7	2.3	8.3	2.5	11.1		
3.0	7.7						

Table C

Distributions of OX Latencies Recorded in the A&C Layers of the Right Geniculate in CHMP Animals

Cat 108		Cat 130		Cat 132		Cat 137	
Latency (msec	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)
0.5	20.0	0.8	5.3	1.8	16.7	0.8	2.6
0.7	20.0	1.0	10.5	1.9	16.7	0.9	5.3
1.3	40.0	1.1	10.5	2.0	16.7	1.0	13.2
1.6	20.0	1.2	10.5	2.5	16.7	1.2	7.9
		1.4	10.5	2.5	16.7	1.3	13.2
		1.6	5.3	2.7	16.7	1.5	7.9
		1.7	10.5	3.0	16.7	1.6	7.9
		1.8	5.3			1.7	10.5
		1.9	10.5			1.8	7.9
		2.0	15.8			1.9	2.6
		2.1	5.3			2.0	5.3
						2.3	10.5
						2.5	5.3

Table D

Distributions of OX Latencies Recorded in the A_1 Layer of the Right Geniculate of CHMP Animals

Cat 108		Cat 130		Cat 132		Cat 137	
Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)
1.0	5.0	0.9	25.0	1.1	20.0	0.7	.5
1.2	30.0	1.0	25.0	1.3	40.0	0.8	4.5
1.3	35.0	1.1	8.3	1.5	40.0	0.9	4.5
1.4	5.0	1.2	8.3			1.0	4.5
1.5	5.0	1.3	8.3			1.1	4.5
1.6	5.0	1.4	8.3			1.2	27.3
1.7	10.0	1.5	8.3			1.3	18.2
2.8	5.0	1.8	8.3			1.5	13.6

Table E

Distributions of OX Latencies Recorded in the A&C Layers of the Right Geniculate in ACMP/BISUT Animals

Cat 188		Cat 190		Cat 191	
Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)
1.0	2.9	0.8	2.4	1.0	6.7
1.1	2.9	0.9	2.4	1.1	3.3
1.2	2.9	1.0	4.8	1.2	13.3
1.3	2.9	1.2	4.8	1.4	3.3
1.4	5.9	1.3	4.8	1.5	3.3
1.5	11.8	1.4	7.1	1.6	3.3
1.6	23.5	1.5	4.8	1.7	16.7
1.7	8.8	1.6	9.5	1.8	6.7
1.8	8.8	1.7	14.3	1.9	6.7
1.9	2.9	1.9	4.8	2.0	6.7
2.0	5.9	2.0	7.1	2.1	10.0
2.2	2.9	2.2	7.1	2.2	3.3
2.3	8.8	2.3	11.9	2.3	3.3
2.4	5.9	2.5	4.8	2.5	6.7
2.5	2.9	2.6	2.4	2.6	3.2
		2.7	7.1	2.8	3.3

Table F

Distributions of OX Latencies Recorded in the A_1 Layer of the Right Geniculate in ACMP/BISUT Animals

Cat 188		Cat 190		Cat 191	
Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)
0.9	5.9	0.9	4.3	1.1	11.8
1.0	2.9	1.0	4.3	1.6	29.4
1.1	5.9	1.2	13.0	1.7	29.4
1.2	5.9	1.3	21.7	1.8	5.9
1.3	11.8	1.4	8.7	1.9	11.8
1.4	17.6	1.5	21.7	2.0	11.8
1.5	29.4	1.6	4.3		
1.6	11.8	1.7	4.3		
1.7	5.9	1.9	4.3		
2.1	2.9	2.0	4.3		
		2.1	8.7		

Table G

Distributions of OX Latencies Recorded in the A&C Layers of the Right Geniculate in CHMP/BISUT Animals

Cat 155		Cat 163		Cat 173		Cat 175	
Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)
1.5	33.3	0.5	2.4	1.0	6.5	0.8	4.5
2.0	33.3	1.0	4.9	1.2	12.9	0.9	9.1
2.1	33.3	1.1	2.4	1.3	9.7	1.0	4.5
		1.2	7.3	1.4	9.7	1.1	13.6
		1.3	14.6	1.5	3.2	1.2	13.6
		1.4	4.9	1.6	22.6	1.3	13.6
		1.5	12.2	1.7	6.5	1.4	9.1
		1.6	12.2	1.8	9.7	1.5	9.1
		1.7	12.2	1.9	6.5	1.6	9.1
		1.8	9.8	2.0	3.2	1.7	4.5
		1.9	4.9	2.2	3.2	3.0	9.1
		2.0	4.9	2.4	3.2		
		2.1	2.4	2.5	3.2		
		2.7	2.4				
		2.8	2.4				

Table H

Distributions of OX Latencies Recorded in the A_1 Layer of the Right Geniculate of CHMP/BISUT Animals

Cat 155		Cat 163		Cat 173		Cat 175	
Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)	Latency (msec)	Rel. Freq. (%)
1.3	12.5	0.8	5.9	1.0	9.1	1.0	11.1
1.7	12.5	1.1	11.8	1.2	18.2	1.1	11.1
1.8	50.0	1.3	5.9	1.3	18.2	1.3	11.1
2.3	12.5	1.5	17.6	1.4	18.2	1.4	33.3
2.5	12.5	1.6	11.8	1.5	18.2	1.5	11.1
		1.8	11.8	1.6	9.1	1.6	11.1
		1.9	5.9	1.7	9.1	2.8	11.1