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The University of North Carolina at Greensboro PH.D. 1984

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RETINAL AND NONRETINAL INFLUENCES ON THE RELATIVE ENCOUNTER RATES FOR X AND Y CELLS IN THE LATERAL GENICULATE NUCLEUS OF THE MONOCULARLY PARALYZED CAT

by

William Guido

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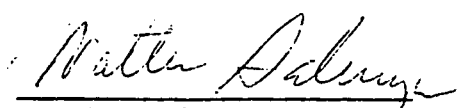

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Brief periods of adult-onset monocular paralysis alter the physiology of the cat lateral geniculate nucleus (LGN) in the thalamus, reducing the encounter rate for X cells relative to that for Y cells. This effect of monocular paralysis is mediated by an active physiologic mechanism which appears sensitive to the disruptions in binocular stimulation brought on by paralyzing the extraocular muscles of one eye. These binocular stimulus modifications include retinally mediated dimensions, such as abnormal patterns of retinal disparity, and nonretinally mediated ones, such as oculomotor/proprioceptive asymmetries. The objective of the present study was to examine which of these sensory modifications (retinal and/or nonretinal dimensions) is necessary to maintain the shift in the X/Y encounter rates produced by monocular paralysis. To accomplish this, retinal and/or nonretinal output arising from the mobile eye of monocularly paralyzed cats was removed by unilateral transection of the optic nerve and/or the ophthalmic branch of the trigeminal nerve, respectively. Standard extracellular recording procedures were used to measure relative encounter rates for X and Y cells from the right and left LGN layers A and A1, before and after the removal of retinal and/or proprioceptive output from one eye. LGN cells were classified as X or Y using a standard battery of receptive field and physiological tests. Removing retinal and/or proprioceptive output, from the mobile eye of monocularly paralyzed cats, resulted in an immediate shift in the encounter rate for X and Y cells in all principal

layers of the LGN. This shift reversed that which had been produced previously by monocular paralysis and restored proportions for these cell types to normal values. Control experiments revealed that these shifts in X/Y encounter rates could not be attributed to deafferentation per se, surgical trauma, or residual surgical anesthesia. Further, the effects of visual and proprioceptive deafferentation were evident in LGN layers innervated by the non-deafferented eye. Thus, these results not only underscore the importance of retinal and proprioceptive output in maintaining the effects of monocular paralysis but also suggest that LGN cells themselves, which previously were thought of as being primarily responsive to monocular stimulation, are apparently quite sensitive to retinal and nonretinal stimulation arising from both eyes.

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CHAPTER I

INTRODUCTION

Early postnatal development of the mammalian visual system is influenced dramatically by visual experience. Alterations in visual stimulation during a "critical period" of development lead to a variety of well known abnormalites in the structure and function of afferent visual pathways from the dorsal lateral geniculate nucleus to striate cortex (see Barlow, 1975; Hirsch & Leventhal, 1978; Movshon & Van Sluyters 1981; Sherman & Spear 1982). Although the mature central nervous system has generally been considered impervious to environmental modification, recent evidence suggests that the period of neural susceptibility to abnormal visual experience may extend beyond the first few months of life and well into adulthood. In cats, both visual cortex (Buchtel, Berlucchi, & Mascetti, 1975; Creutzfeldt & Heggelund, 1975; Fiorentini, & Maffei, 1974; Fiorentini, Maffei, & Bisti, 1979; Maffei, & Fiorentini, 1976) and the dorsal lateral geniculate nucleus (LGN) of the thalamus (Brown & Salinger, 1975; Eysel, Gonzalez-Aguilar, & Mayer, 1980, 1981; Eysel & Mayer, 1979; Hamori & Silakov, 1980; Garraghty, Salinger, MacAvoy, Schroeder, & Guido, 1982; Salinger, Garraghty, MacAvoy, & Hooker, 1980; Salinger, Garraghty, & Schwartz, 1980; Salinger, Schwartz, & Wilkerson, 1977a, 1977b; Salinger, Wilkerson, & MacAvoy, 1977) exhibit a remarkable degree of flexibility in response to certain adult-onset stimulus modifications. Over the years, Salinger

and colleagues have explored the mechanisms underlying the physiological changes which occur in the cat lateral geniculate nucleus (LGN) in response to brief periods of adult-onset monocular paralysis.

LGN: Functional Architecture and Cell Types

The lateral geniculate nucleus of the cat is a laminated structure composed of three principal layers. Optic tract fibers from the contralateral eye project to the dorsal and ventral layers (A & C), while ipsilateral fibers project to the middle layers (Garey & Powell, 1968; Laties & Sprague, 1966; Stone & Hansen, 1966) Guillery (1970) has also described an additional sublamina of the ventral layer which also receives an ipsilateral projection. The projection of retinal fibers onto the LGN is retinotopically organized, with layers aligned so that a line perpendicular to the dorsal surface represents the same region of visual space in the two eyes (Bishop, Kozak, Levick, & Vakkur, 1962; Kaas, Guillery, & Allman, 1972; Sanderson, 1971). Cells of the LGN constitute the first relay of inputs from the retina to visual cortex. Like retinal ganglion cells, LGN cells can also be divided into three types, namely W, X, and Y cells. Much less is known about W cells, but compared to Y cells, X cells tend to have more slowly conducting axons, more linear spatial summation in the receptive field, smaller receptive field size, a greater sensitivity to visual stimuli consisting of higher spatial frequency, a poor sensitivity to visual stimuli with a high temporal frequency, and a more sustained response to visual stimuli of an apparent standing contrast (see Blake, 1979; Lennie, 1980; Sherman & Spear, 1982). Recently, intracellular injections of horseradish peroxidase into physiologically identified LGN

neurons has revealed that X and Y cells possess morphologically distinct features which correspond nicely with the functional differences between these two cell types (Friedlander, Lin, Sherman, 1979; Friedlander, Lin, Stanford, & Sherman, 1981). Finally, these cell groups appear to be links in at least two parallel relatively independent neural chains from retina through LGN and onto visual cortex. It has been suggested that each of these chains analyzes somewhat different features of the visual scene (see Lennie, 1980; Rodieck, 1979; Sherman, 1982; Stone, Dreher, & Leventhal, 1979).

The Effects of Monocular Paralysis in the LGN of an Adult Cat

Brown and Salinger (1975) first reported that two or more weeks (chronic) of monocular paralysis, induced by the surgical transection of cranial nerves III, IV, and VI, substantially reduce the number of X cells relative to Y cells (as defined by receptive field properties), encountered in contralateral LGN laminae innervated by the paralyzed eye. This effect seems dependent upon the duration of the experience, since the distribution of encountered LGN cells obtained from animals that were acutely paralyzed (1-4 days) is comparable to the distribution obtained from normal animals (Hoffmann, Stone, & Sherman, 1972). In a more recent analysis, Salinger et al. (1977b) reported that chronic monocular paralysis produces a substantial reduction in the proportion of LGN cells that exhibit relatively longer latencies in response to optic chiasm (OX) stimulation. Because OX latency values relate closely to LGN X and Y cell classification (Hoffmann, Stone, & Sherman, 1972; Wilson, Rowe, & Stone, 1976; Kratz, Webb, & Sherman 1978), LGN neurons become identifiable as X or Y type on the basis of their response to OX

stimulation (Bullier & Norton 1979; Eysel, Grusser, & Hoffmann, 1979; Garraghty et al., 1982; see Rowe & Stone 1977). Utilizing the OX latency as a means to identify X and Y cells, Salinger et al. (1977b) concluded that X cells are encountered less frequently relative to Y cells in LGN laminae A and C, innervated by paralyzed eye. Further, using this procedure permitted an assessment of the contralateral LGN lamina innervated by the mobile, unoperated eye, where it was revealed that the shift in the encounter rates for X and Y cells was more prominent among lamina A1 cells, driven by the mobile, presumably normal eye, than among cells receiving inputs from the paralyzed eye. More recently, conduction velocity and receptive field classification data confirm, as the OX latency measures indicate, that in the adult, brief periods of monocular paralysis reduce the proportion of encountered X cells relative to Y cells (Garraghty et al., 1982).

The Role of an Active Physiological Process in Mediating the Effects of Monocular Paralysis

In principle, the effects of monocular paralysis could result from either some atrophic or degenerative process secondary to surgical trauma accompanying transection of cranial nerves, or from a tonic physiological inhibition brought about by paralyzing one eye. While a passive, degenerative process might account for the changes in LGN physiology observed in laminae innervated by the paralyzed eye, a more active process would be required to explain the effects observed in LGN laminae innervated by the mobile, unoperated eye (Garraghty et al., 1982; MacAvoy & Salinger 1980; Salinger et al., 1977b). Further, an active mechanism seems more likely in light of the observation that

paralysis of one eye, induced either by cranial nerve section or tenotomization, manipulations that share no apparent surgical risks but result in the same loss of ocular motility, produce comparable effects on LGN physiology (Salinger, Garraghty, MacAvoy, & Hooker, 1980).

Further support for an active physiological mechanism has emerged from studies in which the effects of monocular paralysis are blocked. If the effects of monocular paralysis are mediated by a degenerative process, it should tend to operate independently of patterned visual stimulation. However, denying pattern vision to monocularly paralyzed animals seems sufficient to protect partially the LGN from the effects of monocular paralysis (Salinger, Garraghty, & Schwartz, 1980). Further, complete protective effects have also been demonstated through pharmacological manipulations (Guido, Salinger, & Schroeder, 1982). In this experiment, chronic monocularly paralyzed cats were treated concurrently with intraventricular injections of 6-hydroxydopamine (6-OHDA), a neurotoxin often employed to destroy catecholamine-containing neurons (Jonsson, 1980). Extracellular recordings revealed no difference in X/Y encounter rates between chronic monocularly paralyzed animals treated with 6-OHDA, and treated or untreated normals. In contrast, chronic animals treated with just a vehicle solution exhibited a relative reduction in the encounter rate for X cells comparable to that produced normally by chronic monocular paralysis. It is unlikely that a degenerative process could account for the effects of monocular paralysis if such changes seem to be dependent upon an intact catecholamine system.

Finally, more direct evidence for an active physiological process

has been demonstrated by pharmacological manipulations that result in the immediate restoration of the X/Y cell encounter ratio. The initial reports of Salinger and colleagues, in which the effects of monocular paralysis have been documented, involved subjects which were merely sedated during physiological recording. Recently it has been shown however, that the effects of monocular paralysis are highly susceptible to level of anesthesia. While recording from chronic monocularly paralyzed cats, shifting systematically from sedative to anesthetic concentrations of sodium pentobarbital produced a rapid recovery in the relative recordability of X cells, restoring the X/Y ratio to normal values (Garraghty et al., 1982). This pattern was also apparent when anesthesia was induced with nitrous oxide, a gaseous anesthetic which requires very little time for induction or recovery, and thus permitted one to compare X/Y cell encounter rates generated from identical electrode penetrations while shifting between sedated and anesthetized states. (Schroeder, Salinger, Hoffmann, & Guido, 1984). These results suggest further that neural elements sensitive to sodium pentobarbital as well as nitrous oxide participate in maintaining the tonic physiological suppression of X cells produced by monocular paralysis.

The idea of an active physiological mechanism seems more plausible when one considers the reported sites of central action for sodium pentobarbital and nitrous oxide, and its effect at anesthetic concentrations on brain function. It has been well established that the ascending pathways of the mesencephalic reticular formation of the brainstem are highly susceptible to anesthetic agents. During anesthesia, afferent stimulation loses its normal capacity to evoke EEG,

behavioral, or emotional arousal, as well as block EEG arousal which is normally induced by direct excitation of the ascending reticular system (French, Verzeano, & Magoun, 1953; Darbinjar, Golovchinsky, & Plehotkina, 1971; Cohen, 1975).

Taken together, the experiments on monocularly paralyzed cats which involve pharmacological manipulations suggest that the effects of monocular paralysis are mediated by an active physiological mechanism, and also imply that such a mechanism may be part of a reticulo-thalamic circuit, sensitive to anesthetic agents, and composed in part of catecholamine neurons. This latter speculation is strenghtened further by the following evidence: (1) LGN receives bilateral projections from mesencephalic reticular formation (Bowsher 1970; Ahlsen & Lo, 1982; Hughes & Mullikin, 1984; Leger, Sakai, Salvert, Touret, & Jouvet, 1975); (2) catecholamine projections that originate in the locus coreuleus complex of the brainstem overlap substantially with ascending projections of the reticular formation (Chu & Bloom, 1974; MacBride & Sutin, 1976; Maeda, Pin, Salvert, Ligier, & Jouvet, 1973); (3) LGN relay cells are sensitive to both stimulation of mesencephalic reticular formation (Foote, Mordes, Colby, & Harrison, 1977; Fukuda & Stone, 1976; Satinsky, 1968; Singer 1973a, 1973b; Singer & Schmielau, 1976); and locus coeruleus (Nakai & Takaori, 1974; Watabe, Nakai, & Kasamatsu, 1982), (4) ascending connections from brainstem to LGN have been regarded as the anatomical substrate for a variety of nonvisual influences over geniculo-cortical transmission including excitability changes associated with attention and eye movements (see Burke & Cole, 1978; Jeannerod, Kennedy, & Magnin, 1979; Singer 1977); and (5)

electrical stimulation of reticulo-thalamic pathways (Singer, 1982; Singer & Rauschecker, 1982) as well as locus coeruleus complex (Kasamatsu, Watabe, Scholler, & Heggelund, 1983) seem to enhance visual cortical plasticity.

Based on the evidence reviewed, it would seem safe to conclude that the effects of monocular paralysis are mediated by an active physiological mechanism, which at least speculatively, may be part of an ascending reticulo-thalamic circuit sensitive to anesthetics, and in part composed of catecholamine neurons.

The Effects of Monocular Paralysis Involve an Active Physiologic Process which is Sensitive to Binocularly Mediated Interactions

The laminar organization of the LGN, with separate layers for input from the two eyes, suggests a pure monocular transformation of retinal activity through the LGN. Despite this arrangement, many investigators have observed binocular interactions in a great many LGN cells (see Freund, 1973; see Singer, 1977) It is also apparent from research done on monocularly paralyzed cats, that LGN cells are subject to very strong interocular influences. The first indication of this emerged when it was found that the change in relative encounter rates for X and Y cells was reduced in LGN layers innervated by the mobile, unoperated eye (Garraghty et al., 1982; MacAvoy & Salinger, 1980; Salinger et al., 1977b). Additional support for binocular sensitivity has also been demonstrated when these effects were also recorded in all principal laminae of the LGN ipsilateral as well as contralateral to the paralyzed eye (MacAvoy & Salinger, 1980; Garraghty et al., 1982). Thus, the relative shift in X/Y encounter rates produced by monocular paralysis is

apparent in all principal laminae of the LGN of both hemispheres, whether the laminae are innervated by the mobile or paralyzed eye. Further, the effects of monocular paralysis seem confined to portions of the LGN which innervate central, binocular visual space (Garraghty et al., 1982). A systematic sampling of the LGN at various zones of retinal eccentricity (0-2°, 3-5°, 6-20°, 21-45°, monocular segment), revealed that portions of the LGN representing 0-20° of central binocular visual space suffered a reduction in the encounter rate for X cells relative to Y cells, whereas regions of the LGN representing the extreme periphery (21-45° and monocular segment), were unaffected by monocular paralysis. The confinement of these effects to central binocular visual space suggests a strong parallel with central visual defects of some functional amyblyopias which have also been hypothesized to involve an X cell dysfunction (Kirshen & From, 1978; Hess & Jacobs, 1979). Taken together, these observations provide strong support for the idea that the effects of monocular paralysis may be due to the activation of a mechanism which is sensitive to interocular cues, and that this binocularly mediated process affects X and Y cells differentially (Garraghty et al., 1982).

Critical Dimensions of the Sensory Modifications Produced by Monocular Paralysis

The sensory modifications produced by monocular paralysis can be broken up into a variety of stimulus dimensions. It is important to establish which of these dimensions is critical for the changes observed in LGN physiology. First, it appears that the visual and nonvisual sensory modifications associated with asymmetric ocular motility

contribute substantially to the changes in physiology observed in both LGN and visual cortex of monocularly paralyzed cats. For example, extracellular recordings from visual cortex (Maffei & Fiorentini, 1976), and LGN (Salinger, Wilkerson, & MacAvoy, 1977; Wilkerson, Salinger, & MacAvoy, 1977) reveal that such structures are more susceptible to monocular paralysis than binocular paralysis. Additional support for an active physiological mechanism which is sensitive to asymmetric patterns of binocular stimulation is evident from a study in which the effects of chronic monocular paralysis are partially reversed when the mobile eye is subsequently paralyzed just prior to physiological recording (Schroeder & Salinger, 1977).

A second stimulus dimension involves the sensory modifications which arise from either the loss of intrinsic or extrinsic eye muscle mobility. Monocular paralysis, induced by transection of cranial nerves III, IV, and VI, results in the denervation of the intrinsic and extrinsic muscle groups of one eye. Paralysis of the intrinsic muscles of one eye produces a loss of pupillary and accomodative control mechanisms, which results in the production of non-consensual retinal illumination, and a monocularly degraded retinal image. Denervation of the extrinsic muscles of one eye results in the cessation of movement of that eye, and a permanent, variable misalignment of the visual axes. Although monocular paralysis involves the denervation of both the intrinsic and extrinsic muscle groups of the eye, only the sensory modifications arising from paralysis of the extrinsic muscles (i.e., abnormal patterns of retinal disparity and oculomotor/proprioceptive asymmetries) appear necessary to produce the relative shift in LGN X/Y

cell encounter rates (Salinger, Garraghty, MacAvoy, & Hooker, 1980). Paralysis of the intrinsic muscles alone, simulated by topical application of the cycloplegic atropine, to one eye (relaxing the lens and pupil) had no detectable effect on LGN physiology. In contrast, paralysis of the extrinsic eye muscles alone, simulated by tenotomization of the extraocular muscles of one eye (misaligning the visual axes), produced an effect on LGN physiology comparable to that observed following transection of cranial nerves III, IV, and VI. From this experiment one can conclude that disruptions in binocular stimulation, arising from the loss of ocular motility and not from unilateral defocussing and non-consensual illumination, seem necessary and sufficient to alter the recordability of LGN X and Y cells seen after monocular paralysis.

Finally, there are two distinct classes of binocularly relevant sensory modifications that arise from unilateral paralysis of the extrinsic muscles: retinal cues in the form of abnormal retinal disparity, and nonretinal cues in the form of abnormal oculomotor/proprioceptive information. To determine whether disturbances of retinal or nonretinal cues are critical for generating the physiological shift in X/Y encounter rates, Salinger, Garraghty, & Schwartz (1980) denied patterned visual experience (thereby eliminating abnormal retinally mediated cues) by coupling the monocular paralysis experience with bilateral eyelid suture. Comparisons made between monocularly paralyzed animals deprived of visual experience and those that were not deprived of patterned visual experience, revealed that extraretinal cues in the form of oculomotor/proprioceptive asymmetries,

were sufficient to produce a relative shift in the encounter rate for X and Y cells in layers innervated by the paralyzed eye. It would seem, however that in order to perform an accurate component analysis, that is, to assess fully the separate, independent contribution of binocularly relevant retinal and nonretinal cues, the complement of the above study needs to be explored. This could be done by removing nonretinal cues while at the same time maintaining retinal cues. Such an analysis seems plausible when one considers the pathways by which retinal and nonretinal information depart the orbit and enter the brain.

All visual stimuli which impinge on photoreceptors depart the orbit along retinal ganglion cell axons. The long axons of ganglion cells pierce the wall of the eye ball at the optic disc, and form the optic nerve (see Lennie, 1980; see Rodieck, 1979). After a partial crossing in the optic chiasm the fibers continue along the optic tracts, until a substantial number of them ultimately synapse on cells in the lateral geniculate nucleus. Thus, unilateral transection of the optic nerve would effectively prevent retinally mediated cues (abnormal patterns of retinal disparity) from arriving to the LGN, while leaving the transmission of nonretinally mediated cues to the LGN intact.

As the binocular lid suture experiments demonstrated, binocularly relevant distortions in extraretinal information, which arise from the unilateral loss of extraocular muscle motility, play a critical role in producing the effects of monocular paralysis (Salinger, Garraghty, & Salinger, 1980). It is believed that an afferent source of extraretinal input has been recorded along the geniculo-striate pathway (Ashton, Boddy, Donaldson, 1983, in press; Buisseret & Maffei, 1977; Donaldson

& Dixon, 1980). In the cat, extraretinal afferents seem to arise from a rich supply of specialized nerve terminals identified in the extrinsic musculature of the eye (Alvarado-Mallart & Picon-Reymond, 1979; Batini, 1979; Cooper & Fillenz, 1955). Sensory feedback from extraocular muscles which convey movement and position of the eye leaves the orbit along oculomotor nerves III, IV, and VI, enters the brain along the ophthalmic subdivision of the trigeminal nerve (V) (Alvarado-Mallart, Batini, Buisseret-Delmas, & Corvisier, 1975; Batini & Buisseret, 1974; Batini, Buisseret, & Buisseret-Delmas, 1975; Buisseret-Delmas, 1976; Porter & Spencer, 1982) and then terminates in the sensory nuclei of the trigeminal nerve (Alvarado-Mallart, Batini, Buisseret-Delmas, & Corvisier, 1975; Alvarado-Mallart, Batini, Buisseret, Gueritaud, & Horchelle-Bossavit, 1975; Cooper & Fillenz, 1955; Manni, Palmieri, Marini, 1971, 1972, 1974; see also Batini, 1979). Thus, unilateral transection of the ophthalmic branch of trigeminal nerve (V) would effectively eliminate distortions in binocular stimulation which arise from nonretinal cues (i.e., proprioceptive asymmetries), while having no impact on the transmission of retinally mediated information.

Purpose of the Present Study

It seems that the effects of monocular paralysis are due to the activation of a physiological mechanism which is sensitive to interocular cues (both retinally and nonretinally mediated ones), and that this binocularly mediated process seems to be capable of modulating the recordability of X and Y cells. If true, then eliminating the source of these retinally and nonretinally mediated cues alone or in combination, may release the tonic shift on the X/Y ratio normally

induced by monocular paralysis, and thereby restore the X/Y ratio to normal values. The objective of the present study was to examine the specific binocular stimulus dimensions associated with monocular paralysis that are necessary to maintain its effect in the LGN. A direct way to assess this was to combine the monocular paralysis preparation with the subsequent removal of either retinal and/or proprioceptive output arising from the mobile eye, accomplished by unilateral transection of the optic nerve and/or ophthalmic branch of trigeminal nerve, respectively.

CHAPTER II

METHOD

Subjects, Experimental Conditions, and General Procedure

The left eyes of 20 adult cats were paralyzed by surgical transection of cranial nerves III, IV, and VI. Of these, 4 were acutely paralyzed (1-4 days) and the remaining 16 were chronically paralyzed (two or more weeks). After this initial period of monocular paralysis, of the 16 chronically paralyzed animals, 4 then had proprioceptive output removed from the mobile eye by unilateral transection of the ophthalmic branch of the trigeminal nerve (V), 4 had retinal output removed from the mobile eye by unilateral transection of the optic nerve (II), 4 had both retinal and proprioceptive output removed from the mobile eye by the combined transection of the optic nerve and the ophthalmic branch of the trigeminal nerve (II+V), and 4 had proprioceptive output removed from the paralyzed eye (V). All 4 of the acutely paralyzed animals had both retinal and proprioceptive output removed from the mobile eye (II+V).

Relative encounter rates of X and Y LGN cells were obtained from each animal in two phases. The first phase of recording was conducted after a period of monocular paralysis. For chronic animals the initial recording session commenced two or more weeks after monocular paralysis surgery, and for the acute animals the initial recording session began within 1-4 days after monocular paralysis surgery. In the first phase

of recording in which animals were monocularly paralyzed, data were collected in two ways. First, a successive pair of penetrations were made through the LGN in virtually the same electrode tract. During one penetration of the pair the animal was sedated, while for the other penetration the animal was anesthetized (order counterbalanced across animals). In order to minimize the extent to which tissue variance (e.g. sampling cells at varying retinal eccentricities) could contribute to changes in the sampling ratio of X and Y cells, sedated and anesthetized pairs were made in virtually the same electrode tract simply by retracting the electrode into the lateral ventricle above the LGN between passes within a given pair. It has been well established that shifting from sedation to anesthesia reverses the effects of chronic monocular paralysis (Garraghty et al., 1982; Schroeder et al., 1984). Therefore, recording sedated-anesthetized pairs from monocularly paralyzed animals permitted an opportunity to obtain a within-animal referent to estimate the extent of recovery one might expect once output from one eye was removed. One or more penetrations were additionally made prior to the removal of II and/or V in which the monocularly paralyzed animal was sedated and not anesthetized. Data collected in this fashion served as an additional baseline to assess whether a recovery had occurred subsequent to the removal of cranial nerves II and/or V.

At the completion of the initial recording phase, the monocularly paralyzed animals were anesthetized, and cranial nerves II, V, or II+V were unilaterally transected. The second recording phase commenced immediately following the avulsion of II and/or V. Sampling rates of

LGN cells were then grouped into the following 5 hour time bins: 0-5 hrs, 5-10 hrs, 20-25 hrs, 25-30 hrs, 30-35 hrs, 40-45 hrs, 45-50hrs, and 95-100 hrs. Within a 5-hour interval, it was possible to make 1-4 penetrations through the LGN.

Surgical Transection of Cranial Nerves

Monocular paralysis was accomplished by unilateral transection of the left cranial nerves III, IV, and VI. This form of surgery involves a ventral approach through the soft palate, and the sphenoid sinus, intercepting the cranial nerves at the common point of entry into the orbit. This procedure permits visualization of the nerves as they course between the cranium and the orbit, lateral and ventral to optic chiasm. The bony covering of optic nerve (II), and the dural covering of the cerebrum remain intact, thus minimizing the risk of accidental damage to the eye, optic nerve, or central visual structures.

Eliminating retinal and/or proprioceptive afferents from one eye was accomplished using a similar ventral surgical approach. For the exposure and avulsion of the optic nerve, the bony covering of optic chiasm and orbit were left intact. For the removal of proprioceptive afferents, the ophthalmic branch of the trigeminal nerve (V) and the semilunar ganglion were exposed and the ophthalmic branch sectioned. The orbit and its contents remained intact and shielded by bone.

Electrophysiological Recording: Preparations and Procedures

Once monocularly paralyzed, animals were anesthetized, placed in a stereotaxic apparatus, and prepared for single unit recording of LGN cells. The skull was exposed and three anchoring screws were implanted

just beneath the cranium. A pedestal, made of dental acrylic cement and containing three large bolts, was built around the three anchoring screws. The pedestal and bolts allow for the animal to be securely mounted in the stereotaxic plane without recourse to painful eye and ear bars. Craniotomies were made over optic chiasm, and left or right optic tract and LGN. Bipolar electrodes, made of Teflon-coated stainless steel, were implanted in optic chiasm (2 mm lateral from midline) and optic tract (about 10 mm from the chiasm electrode) using electrophysiological criteria. The exact placement of each stimulating electrode was verified histologically.

At the beginning of each recording session, animals were sedated and placed into the stereotaxic apparatus. The position of the left optic disc (paralyzed eye) was projected and mapped on a tangent screen at least one meter from the orbit. Receptive field locations of the paralyzed eye were mapped with respect to this landmark (Fernald & Chase, 1971). Receptive field positions for cells innervated by the mobile eye were estimated from field positions of cells recorded in adjacent laminae and innervated by the paralyzed eye, since it is known that visual maps of these laminae are in register (Bishop et al., 1962; Kaas et al., 1972; Sanderson, 1971). Data were taken only from cells within the central 10 degrees of visual space and from LGN laminae A and A1. During recording sessions, which lasted 8-12 hours a day, both eyes were protected with plano contact lenses, and temperature and respiration were monitored and maintained within normal physiological limits.

Action potentials of LGN cells were isolated with tungsten

microelectrodes (10-20ΛM at 1000 Hz.) The signals were amplified with a WPI DAM-5 preamplifier and Grass AC amplifier, and displayed on a Textronix storage oscilloscope. LGN cell body unit activity was distinguished from axon unit activity using the criteria described by Hubel (1960) and Bishop, Burke & Davis (1962). The electrode was advanced slowly in 3-4 um steps through the LGN while searching for isolated units. Visually responsive units were isolated during microelectrode penetrations using stroboscopic flashes, and with hand-held wands and gratings moved across the line of sight. Since some conditions resulted in the visual deafferentation of LGN cells an addtional search strategy was employed. Under such circumstances deafferented units can not receive direct retinal input. However, frequently stroboscopic flashes were able to drive LGN cells in the visually deafferented layers, with the onset of response to the flash starting several hundred milliseconds later than a cells' typical response to direct retinal stimulation. In the event that not all cells in the deafferented layers were responding to the flash, unit activity was sampled every 100 um, and electrical properties of the cell was assessed (see below), regardless of the cells' ability to respond to the flash.

Electrical stimulation of optic chiasm (OX) and optic tract (OT) consisted of 0-15 volt square wave pulses delivered at a duration of 10-100 us, from a Grass 8 stimulator at a rate of 1 Hz, through a stimulus isolation unit. The latency of an action potential recorded in the LGN represented the time it took for a stimulating pulse (triggered by OX or OT stimulation) to reach and drive an LGN cell. Since the

distance between OX and OT electrodes was actually measured at the completion of the experiment, recording response latencies to OX and OT stimulation permitted the computation of afferent axonal conduction velocity. LGN relay cells which are innervated by rapidly conducting afferents (> 25 meters/second) are typically classified as Y type, while LGN relay cells innervated by slowly conducting afferents ($\leq$ 25 meters/second) are typically classified as X type (Cleland, Dubin, & Levick 1971b; Fukada, 1971; Garraghty et al., 1982; So & Shapely, 1979).

In addition to conduction velocity a standard battery of four receptive field tests was conducted on all cells innervated by the paralyzed eye. Since animals were not paralyzed systemically, it was not possible to examine receptive field properties of cells innervated by the mobile eye. Cells innervated by the paralyzed eye were classified as having X or Y type receptive field properties on the basis of (1) receptive field center diameter (X: $\leq$1.00 degree, Y>1.00 degree), (2) response to moving gratings (X: failure to respond to any spatial frequency at high temporal frequency, Y: response burst at high temporal frequency), (3) response to a rapidly moving center-inhibiting stimulus larger than the field center (X: no response, Y: response), and (4) degree of center-surround antagonism (X: strong antagonism, Y: weak or no antagonism) (Bullier & Norton, 1979; Eysel et al., 1979; Geisert, Spear, Zetlan, & Langsetmo, 1982; Hoffmann et al., 1972; Kratz et al., 1978; Wilson et al., 1976).

Based on the classification scheme consisting of conduction velocity and four receptive field measures, a cell innervated by the

paralyzed eye was identified as X or Y if no more than one test disagreed with the others. In the monocularly paralyzed cat, the correspondence between conduction velocity and other classification criteria generally exceeds 95% (Garraghty et al., 1982). Cells in which more than one test disagreed with the others were identified as having mixed properties and designated as unclassified cells. Cells innervated by the mobile eye were classified as X or Y only on the basis of conduction velocity measurements. Therefore, only cells innervated by the paralyzed eye could conceivably be designated as unclassified.

Safeguards Against Pain and Discomfort

All animals undergoing surgery were deeply anesthetized. Surgical anesthesia, or stage III, plane 2 anesthesia, is determined by (1) the absence of nociceptive reflexes, (2) the absence of a corneal blink and tendon reflexes, and (3) abdominal instigation of the inspiratory phase of respiration (Cohen, 1975). While anesthetized, or while recovering from the effects of anesthesia, an animal's temperature and respiration were monitored, and maintained within normal physiological limits.

Animals undergoing surgery two or more weeks before an electrophysiological recording session were anesthetized with intraperitoneal injections of a mixture of acepromazine maleate (2.9 mg/kg) and sodium pentobarbital (5.0 mg/kg). Supplemental doses of sodium pentobarbital (5.0 mg/kg) were given to maintain animals in a state of plane III, stage 2 anesthesia. For surgery scheduled 0-2 hrs before a recording session, and for those recording sessions in which animals were required by experimental design to be anesthetized, anesthesia was induced by inhalation of a mixture of nitrous oxide (20%)

and oxygen (80%) after pretreatment with a mixture of acepromazine maleate (2.9 mg/kg) and sodium pentobarbital (5.0 mg/kg).

During recording sessions in which the animal was to be recorded while sedated but not anesthetized, animals were administered intraperitoneal injections of a mixture of acepromazine maleate (2.9 mg/kg) and sodium pentobarbital (5.0 mg/kg). Sedated animals are able to accept painless head restraint by means of a skull-mounted acrylic pedestal. Sedated animals retained the following responses: nociceptive reflexes, normal respiration and temperature, visual tracking of the mobile eye during recording, capability of ataxic locomotion upon release from head restraint, and an ability to feed following a recording session. Animals in this state are free to move (except the head) if they are merely restless, much less in pain. Since it is impossible to record from isolated LGN units if the animal does not remain absolutely quiescent, these limitations in the recording procedures constitute an effective safeguard against pain and discomfort.

At the completion of the experiment all animals were sacrificed with an overdose injection of the anesthetic sodium pentobarbital (70-80 mg/kg), and perfused first with saline, and then with a formal-saline solution. The brains were then extracted for histological purposes.

Statistical Methods

Relative encounter rates for LGN cells (X, Y, and unclassified) were obtained from monocularly paralyzed animals in two phases, prior to and immediately following the removal of retinal and/or proprioceptive output from one eye. During the first recording phase, encounter rates

were derived first from a pair of successive penetrations made in virtually the same electrode track in which the animal was sedated during one penetration and then anesthetized for the other, and secondly, from one or more penetrations in adjacent electrode tracks in which the animal was merely sedated. During the second phase of recording in which retinal and/or proprioceptive output from one eye was removed, relative encounter rates were measured and grouped into 5-hour bins.

Using each cat as the unit of observation, an analysis of variance was performed on the relative enounter rates for LGN cells recorded under sedated recording conditons prior to and after the removal of retinal and/or proprioceptive output from one eye. In order to determine whether the removal of retinal and/or proprioceptive output from one eye had an effect on layers innervated by one or the other eye, separate analyses were performed on data collected from layers innervated by the paralyzed eye and for layers innervated by the mobile eye. The between-group factor consisted of the actual experimental conditions (1 group of acutely paralyzed cats in which II+V from the mobile eye was removed, and 4 groups of chronically paralyzed animals in which II, V, or II and V were removed from the mobile eye or V removed from the paralyzed eye). The within-group factors consisted of the actual recording time (before and at 0-5 hrs, 5-10 hrs, 20-25 hrs, and 25-30 hrs after output from one eye was removed, and cell type (X, Y, and unclassfied cells for the analysis conducted on the paralyzed eye, and X and Y cells for the analysis on the mobile eye).

Because it was sometimes difficult to locate the LGN and then to

sample cells only in areas innervating the central ten degrees of visual space, it was not always possible to obtain relative encounter rates for a given animal at each of the recording times included in the analysis. When this occurred a derived score was calculated, which was based on the relative frequency of a cell type obtained for a given experimental condition rather than for a given subject. With a matrix that consisted of 600 possible entries, the number of synthetic entries was less than 10% (20 for the paralyzed eye and 36 for the mobile eye). Derived scores were used only to facilitate the analysis of variance (Keppel, 1982) and were not included for any summaries of data which appeared in figures.

Planned comparisons involving simple interactions, simple main effects, and simple comparisons were performed using F tests with corrected alpha levels (Keppel, 1982). Summary tables for all statistics are presented in Appendix A.

Although relative encounter rates were also obtained in the initial recording phase under anesthesia (for sedated-anesthetized pairs) and in the second recording phase for times beyond 35 hours, these data were excluded from the analysis of variance. Sedated-anesthetized pairs were used as a within animal referent, to estimate the extent of recovery one might expect once retinal and/or proprioceptive output from one eye was removed. The average percentage of change which occurred between encounter rates was calculated for the sedated-anesthetized pairs and compared with the average percentage of change in encounter rates which occurred once retinal and/or proprioceptive output from one eye was removed, using a Wilcoxon matched-pairs signed-ranks test (Daniel,

1978). Relative encounter rates obtained beyond 30 hours were also excluded from the analysis of variance since it was not always feasible to obtain data for each animal at such times. However, these data were used anecdotally, to relate to the issue of the stability of an effect produced by retinal and/or proprioceptive deafferentation.

CHAPTER III

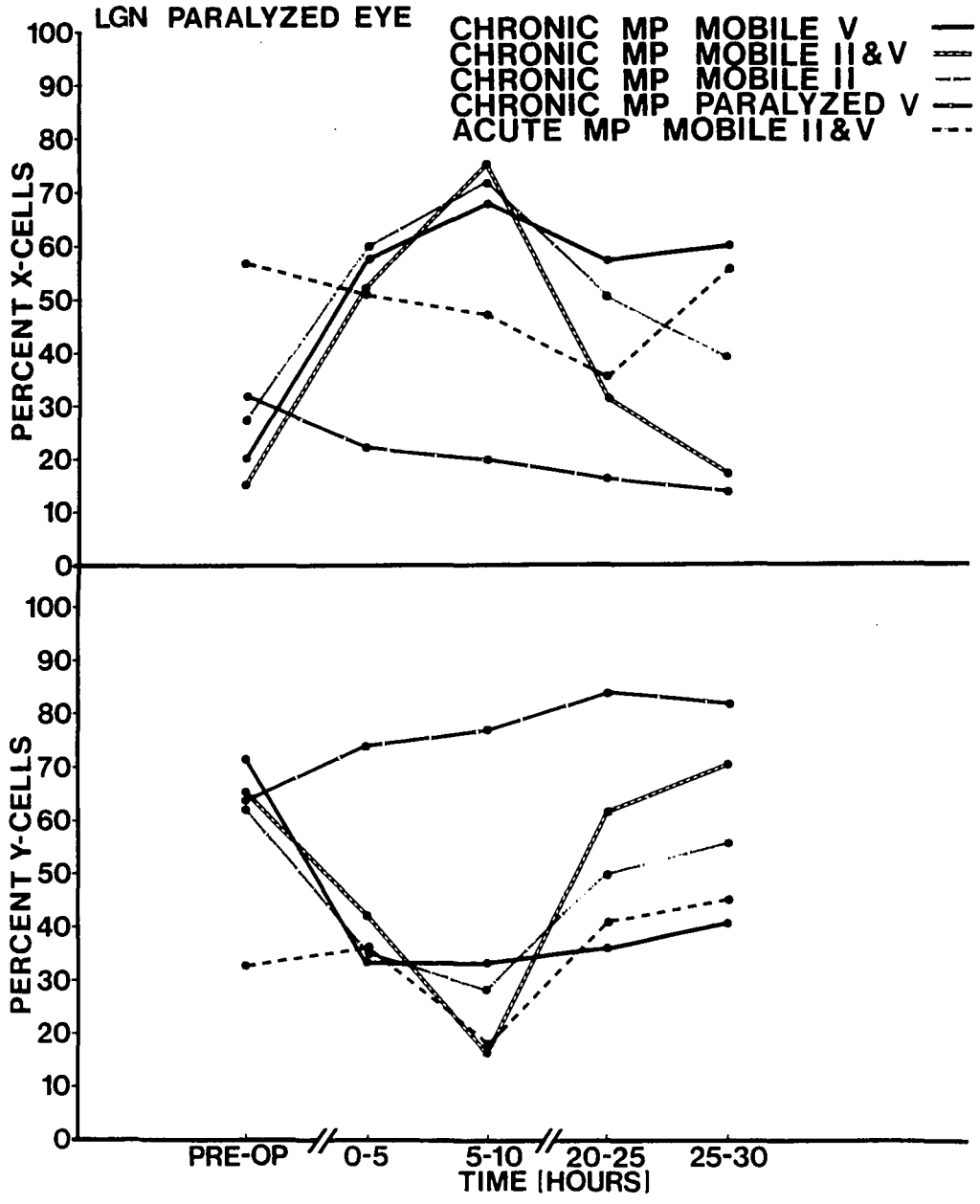
RESULTS

For 20 animals, the relative encounter rates for LGN cells were measured during two phases: the first, after an initial period of monocular paralysis (1-4 days for 4 acutely paralyzed animals, and two or more weeks for the 16 chronically paralyzed animals) and then again immediately following the removal of either II, V, or II+V from one eye. During the first recording phase, when animals were monocularly paralyzed, data were obtained, first, by making a pair of successive penetrations in the same location of the LGN in which one penetration was conducted while the animal was sedated and the other while the animal was anesthetized, and second, by making one or more adjacent penetrations through the LGN while the animal was merely sedated. During the second recording phase, which began immediately following the removal II, V, or II+V from one eye, data were obtained under sedated recording conditions and grouped in 5 hour time bins. Extracellular recordings were made from 1336 cells in either the right or left LGN in laminae A and A1, from portions representing the central 10 degrees of visual space.

Between-Group Analyses

Figure 1 presents data for each of the five experimental conditions collected from LGN layers innervated by the paralyzed eye. It displays

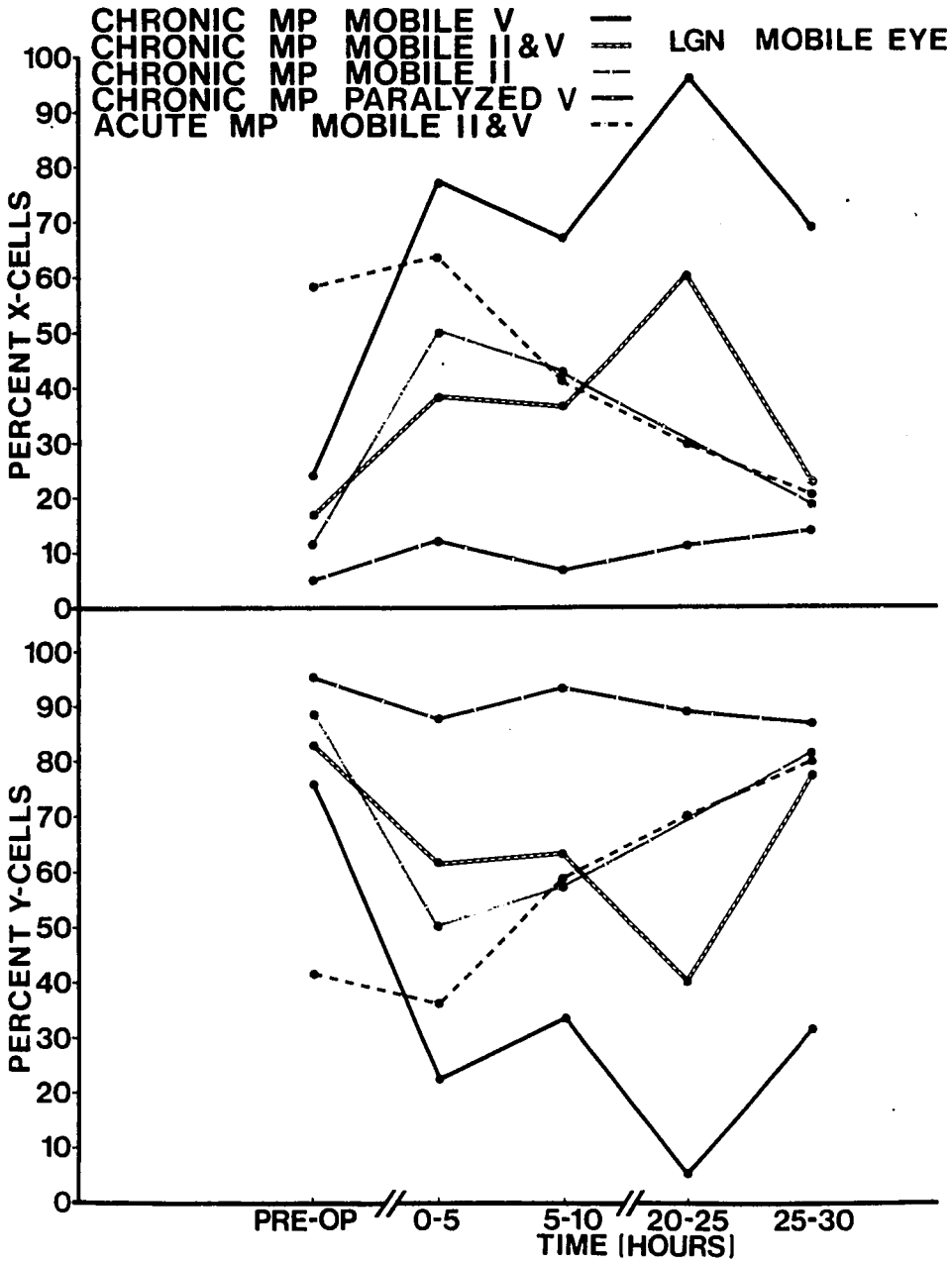
Figure 1. Relative percentages of X and Y cells encountered in LGN layers innervated by the paralyzed eye for each of the five experimental conditions, which included one group of acutely paralyzed animals in which retinal and proprioceptive output was removed from the mobile eye (Acute MP Mobile II+V) three groups of chronically paralyzed animals in which retinal (Chronic MP Mobile II) or proprioceptive (Chronic MP Mobile V) or both retinal and proprioceptive (Chronic MP Mobile II+V) output was removed from the mobile eye, and one group of chronically paralyzed animals in which proprioceptive output was removed from the paralyzed eye (Chronic MP Paralyzed V). Each experimental group contained four cats. The ordinate displays the relative percentages of X cells (top) and Y cells (bottom) encountered in complete penetrations made through the right or left LGN layers A and A1. The abscissa indicates the times when data were collected, namely, prior to (pre-op) or at 0-5 hrs, 5-10 hrs, 20-25 hrs, and 25-30 hrs after the removal of output from one eye.


LGN PARALYZED EYE
CHRONIC MP MOBILE V
CHRONIC MP MOBILE II&V
CHRONIC MP MOBILE II
CHRONIC MP PARALYZED V
ACUTE MP MOBILE II&V
PERCENT X-CELLS
PERCENT Y-CELLS
100
90
80
70
60
50
40
30
20
10
0
PRE-OP
0-5
5-10
20-25
25-30
TIME (HOURS)

the relative percentages of X and Y cells recorded before and 0-5, 5-10, 20-25, and 25-30 hrs after the removal of retinal and/or proprioceptive output from one eye. The analysis of variance performed on the relative frequency of X, Y, and unclassified cells indicated a significant interaction ($p<.0001$) between experimental condition (one group of acutely paralyzed cats in which II+V were removed from the mobile eye, three groups of chronically paralyzed cats in which II, V, or II+V were removed from the mobile eye, and one group of chronically paralyzed cats in which V was removed from the paralyzed eye), recording times (preop, 0-5 hrs, 5-10 hrs, 20-25 hrs, 25-30 hrs), and cell type (X, Y, and unclassified cells). Thus, in at least one of five experimental conditions significant changes in one or more cell types occurred at one or more times of recording. The simple interaction between experimental condition and time of recording for X, Y, and unclassified cells was significant for X cells ($p<.01$) and Y cells ($p<.01$) but was not significant for unclassified cells. Since the percentage of unclassified cells did not change significantly for any condition, at any time of recording, it was unlikely that encounter rates for X and Y cells were changing due to a relative increase in the encounter rate for unclassified cells. Thus, conditions which increased the encounter rate for X cells also resulted in a roughly corresponding decrease in that for Y cells.

Figure 2 presents data for each of the five experimental conditions collected from LGN layers innervated by the mobile eye. It displays the relative percentages of X and Y cells before and 0-5, 5-10, 20-25, 25-30 hrs after the removal of output from one eye. The analysis of variance

Figure 2. Relative percentages of X and Y cells encountered in LGN layers innervated by the mobile eye for each of the five experimental conditions, which included one group of acutely paralyzed animals in which retinal and proprioceptive output was removed from the mobile eye (Acute MP Mobile II+V), three groups of chronically paralyzed animals in which retinal (Chronic MP Mobile II), or proprioceptive (Chronic MP Mobile V), or both retinal and proprioceptive (Chronic MP Mobile II+V) output was removed from the mobile eye, and one group of chronically paralyzed animals in which proprioceptive output was removed from the paralyzed eye (Chronic MP Paralyzed V). The ordinate displays the relative percentages of X cells (top) and Y cells (bottom) encountered in complete penetrations made through the right or left LGN layers A and A1. The abscissa indicates the times when data were collected, namely, prior to (pre-op) or at 0-5 hrs, 5-10 hrs, 20-25 hrs, and 25-30 hrs after the removal of output from one eye.


CHRONIC MP MOBILE V
CHRONIC MP MOBILE II&V
CHRONIC MP MOBILE II
CHRONIC MP PARALYZED V
ACUTE MP MOBILE II&V
LGN MOBILE EYE
PERCENT X-CELLS
PERCENT Y-CELLS
100
90
80
70
60
50
40
30
20
10
0
PRE-OP
0-5
5-10
20-25
25-30
TIME (HOURS)

performed on the relative frequency of X and Y cells indicated a significant interaction between experimental condition, time of recording, and cell type ($p<.002$). Thus, in at least one of five conditions significant changes in the encounter rate of one or more cell types occurred at one or more times of recording. The simple interaction between condition and time of recording was significant for both X ($p<.01$) and Y cells ($p<.01$). Since it was not possible to identify unclassified cells in layers innervated by the mobile eye (see Methods), a condition which increased the encounter rate for X cells also, of neccessity, resulted in a corresponding decrease in that for Y cells.

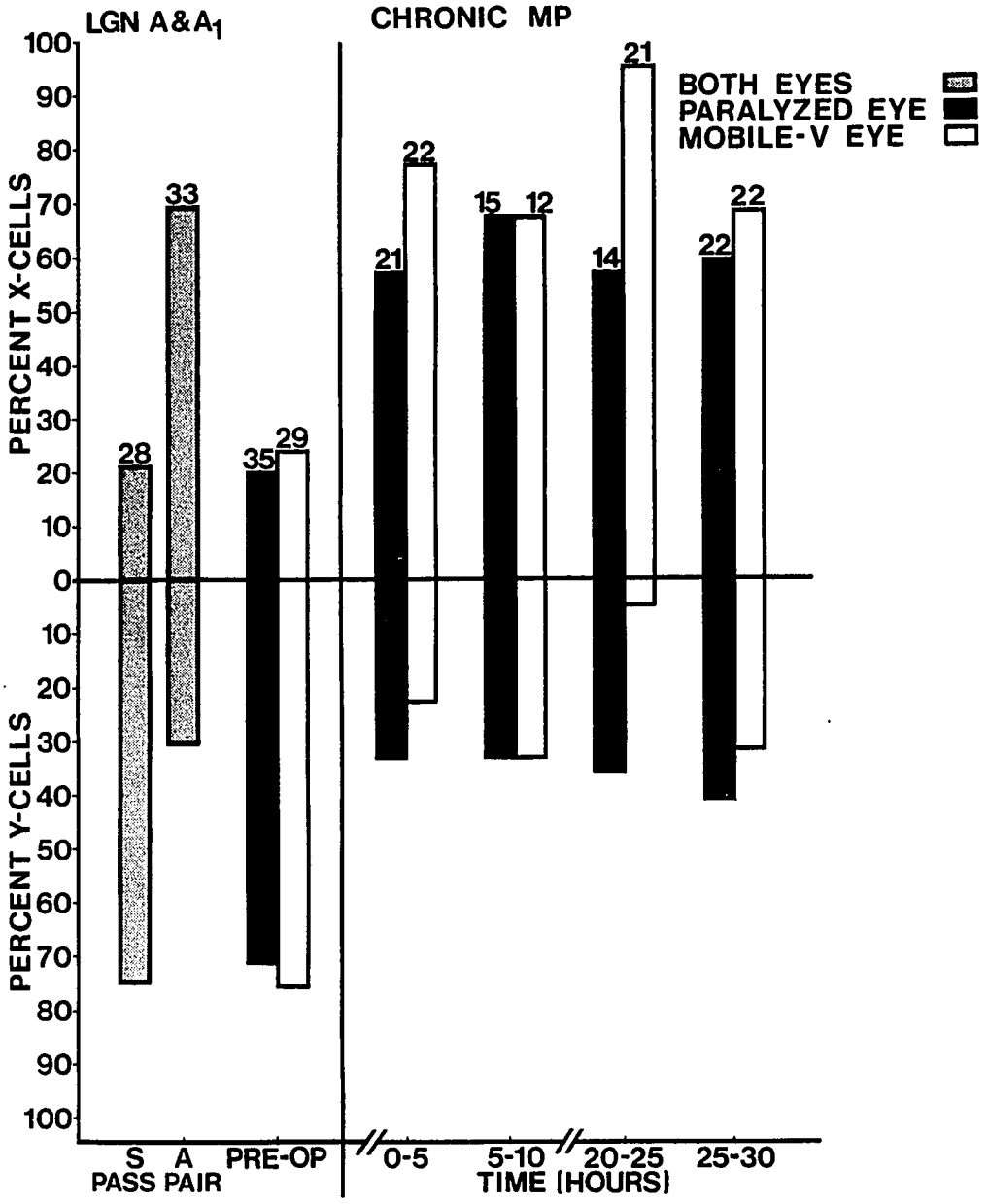
Within-Group Comparisons

Within each of the five experimental conditions, three aspects of the data were examined. First, it was investigated whether the removal of proprioceptive and/or retinal output from one eye resulted in a recovery in the encounter rate for X and Y cells. Since brief periods of monocular paralysis produce a significant decline in the encounter rate for X cells and a corresponding increase in that for Y cells, a recovery occurring after the removal of II and/or V would result in a relative increase in the encounter rate for X cells and a corresponding decrease in that for Y cells. Significant changes in encounter rates were examined, first by testing for simple main effects comparing the relative frequencies of X and Y cells recorded under sedated recording conditions, before and 0-5, 5-10, 20-25, and 25-30 hrs after output from one eye was removed, and second, by making simple comparisons, comparing values recorded at the times listed above. Second, if a change was

apparent in these latter comparisons, the duration of such a recovery was examined by means of additional simple comparisons made between early and late postoperative time bins. Third, if the removal of output resulted in a recovery from the effects of chronic monocular paralysis, the extent to which such a recovery could be judged as "complete" was examined by comparing the average amount of recovery observed once II and/or V was removed with that obtained from the same animal, by shifting from sedation to anesthesia through the use of Wilcoxon matched-pairs signed-ranks test.

The removal of V from the mobile eye of chronically paralyzed cats. Figure 3 presents the relative percentages of X and Y cells recorded from 4 chronically monocularly paralyzed cats prior to and after the removal of proprioceptive output (V) from the mobile eye. The ordinate displays the relative precentages of X (top) and Y (bottom) cells encountered in complete penetrations through either the left or right LGN layers A and A1. The left hand panel presents grouped data collected before V (preop) was removed. The stipled bars represent data collected from A and A1 collectively from 4 pairs (one from each cat) of successive penetrations made through the LGN, in which the animal was sedated (S) during one penetration and anesthetized (A) during the other (pass-pair). These data are collapsed across layers because anesthesia affects the recordability of LGN cells independently of the cells source of innervation (Garraghty et al., 1982; Schroeder et al., 1984). The dark and light bars reflect data obtained under sedated recording conditions, with the dark bars representing cells encountered in layers innervated by the paralyzed eye (rLGN lamina A, lLGN lamina A1) and the

Figure 3. The relative percentages of X and Y cells recorded from four chronically paralyzed animals before and after the removal of proprioceptive output (V) from the mobile eye. The ordinate displays the relative percentages of X cells (top) and Y cells (bottom) encountered in complete penetrations made through the right or left LGN layers A and A1. The left hand panel presents data obtained prior to the removal of V. The stipled bars present the relative percentages of X and Y cells encountered in A and A1 collectively, for sedated (S) and anesthetized (A) pairs of successive electrode penetrations (pass-pairs). The dark and light bars present the relative percentages of cells encountered under sedated recording conditions with the dark bars representing LGN layers innervated by the paralyzed eye and the light bars representing LGN layers innervated by the mobile eye. The numbers above each bar indicate absolute cell frequencies. The right hand panel presents data obtained from these same animals at 0-5 hrs, 5-10 hrs, 20-25 hrs, and 25-30 hrs after proprioceptive deafferentation.


LGN A&A1
CHRONIC MP
BOTH EYES
PARALYZED EYE
MOBILE-V EYE
PERCENT X-CELLS
PERCENT Y-CELLS
100
90
80
70
60
50
40
30
20
10
0
10
20
30
40
50
60
70
80
90
100
28
33
35
29
21
22
15
12
14
21
22
22
S A
PASS PAIR
PRE-OP
0-5
5-10
20-25
25-30
TIME (HOURS)

light bars representing cells encountered in layers innervated by the mobile eye (rLGN layer A1, lLGN layer A). These data are separated by laminae in order to examine the the possibility that the removal of output from one eye produces interocular effects. The right hand panel displays grouped data from these same animals, again separated by laminae, at 0-5 hrs, 5-10 hrs 20-25 hrs and 25-30 hrs after proprioceptive output was removed from the mobile eye. The numbers above each bar represent absolute cell frequencies.

For layers innervated by the paralyzed eye, the percentage of X cells recorded before the removal of V (preop) was 20%, compared to values of 57.1% at 0-5 hrs, 67.7% at 5-10 hrs, 57.1% at 20-25 hrs, and 59.1% at 25-30 hrs. The percentage of Y cells recorded preoperatively was 71.4%, compared to postoperative values of 33.3% at 0-5 hrs, 33.3% at 5-10 hrs, 35.7% at 20-25 hrs, and 40.9% at 25-30 hrs. Significant changes in the encounter rate for X cells ($p<.01$) and Y cells ($p<.01$) occurred at one or more times of recording (simple main effect of time). Simple comparisons made between values recorded before and after (0-5 hrs, and 5-10 hrs) the removal of V indicated that these changes were the result of a significant increase in the encounter for X cells ($p<.01$) and corresponding decrease in that for Y cells ($p<.01$), a shift in the X/Y ratio which reflects a recovery from the effects of chronic monocular paralysis. Further, there were no differences between values recorded at 0-5 hrs and any time thereafter, which suggests that the shift remained stable through at least 30 hrs.

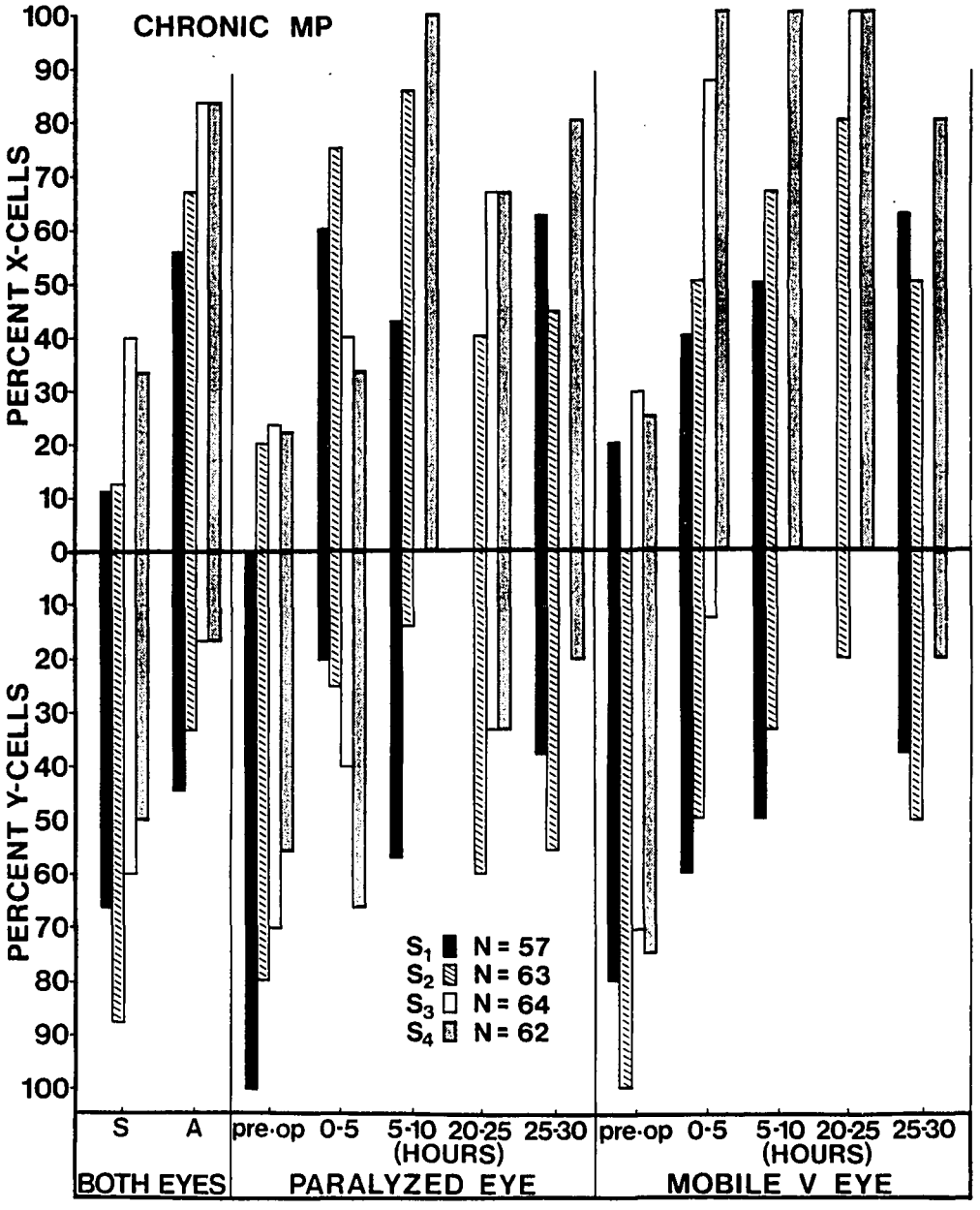
For layers innervated by the mobile eye the percentage of X cells recorded before the removal of V was 24.1% compared to postoperative

values of 77.3% at 0-5 hrs, 66.7% at 5-10 hrs, 95.2% at 20-25 hrs, and 68.2% at 25-30 hrs. The percentage of Y cells recorded before the removal of V was 75.8% compared 22.7% at 0-5 hrs, 33.3% at 5-10 hrs, 4.8% at 20-25 hrs, and 31.8% at 25-30 hrs. Significant changes in the encounter rate for X cells ($p<.01$) and Y cells ($p<.01$) occurred at one or more times of recording (simple main effect of time). Simple comparisons made between values recorded before and at each postoperative time bin indicated that these changes were the result of a significant increase in the encounter rate for X cells ($p<.01$) and a corresponding decrease in that for Y cells ($p<.01$), a pattern which remained in effect through 30 hrs.

Individual data displayed in Figure 4 indicated that the relationships observed in the grouped data occurred consistently in each of the 4 cats tested. Individual encounter rates for a given time of recording were based on cell frequencies ranging from 1-17. Such cell frequencies are substantially smaller than those associated with grouped encounter rates, but nonetheless, seemed sufficient to provide a surprisingly reliable estimate of cell recordability.

In an attempt to examine whether the recovery observed through 30 hrs persisted, data were obtained in some animals as late as 100 hrs (see Appendix B for all data collected after 30 hrs). Although excluded from the analysis, values obtained at 30-35 hrs, 40-45 hrs, 45-50 hrs, and 95-100 hrs resembled values recorded between 0-30 hrs, and suggest that the removal of proprioceptive output from the mobile eye resulted in a long-lasting and stable recovery, persisting well beyond the time period which was sampled systematically.

Figure 4. Relative percentages of X and Y cells displayed individually for four chronically paralyzed animals before and after the removal of proprioceptive output (V) from the mobile eye. Relative precentages for X and Y cells are presented for each of the four animals tested, first, for sedated (S) and anesthetized (A) pairs of successive electrode penetrations which were obtained prior to the removal of V, and then separately for layers innervated by the paralyzed eye and for layers innervated by the mobile eye, before (pre-op) and at 0-5 hrs, 5-10 hrs 20-25 hrs, and 25-30 hrs after the removal of V.


CHRONIC MP
PERCENT X-CELLS
PERCENT Y-CELLS
100
90
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0
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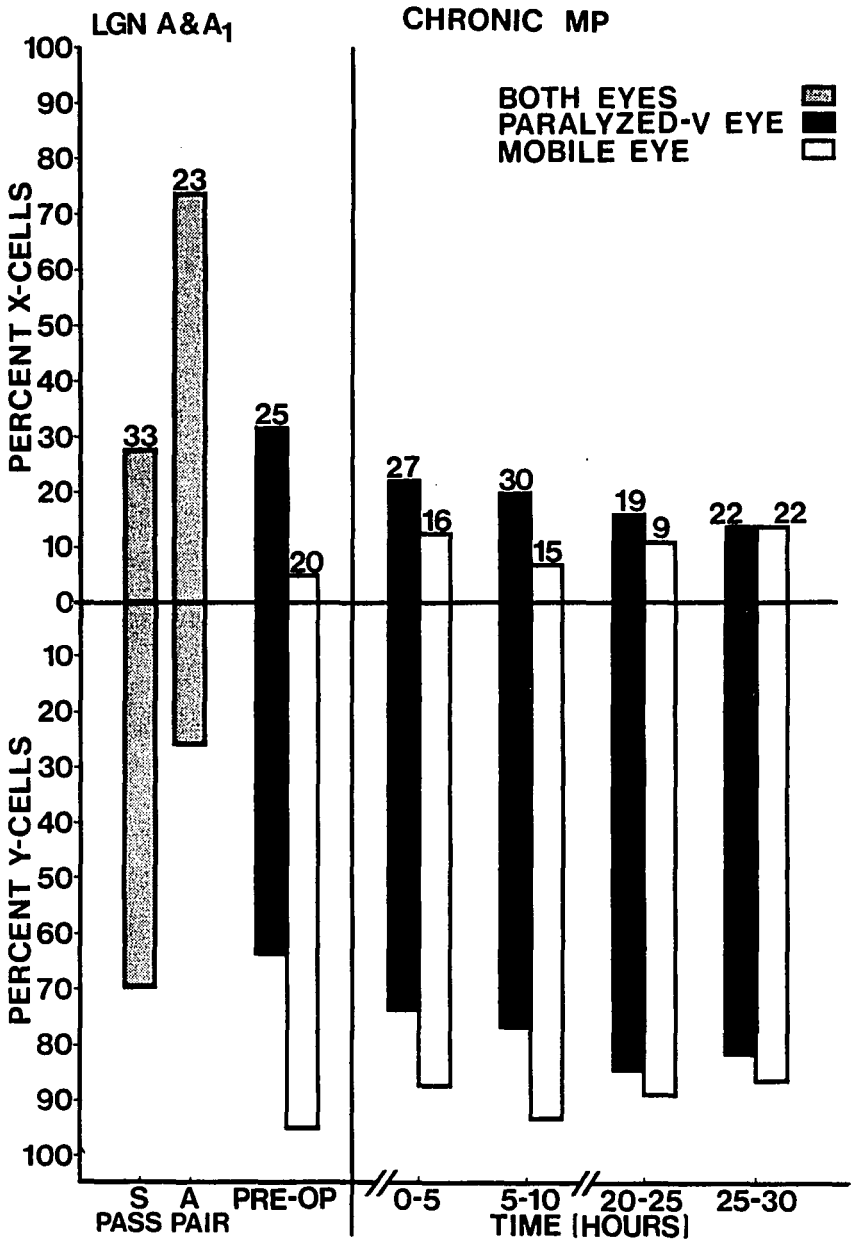
60
70
80
90
100
S
A
pre-op
0-5
5-10
20-25
25-30
(HOURS)
pre-op
0-5
5-10
20-25
25-30
(HOURS)
BOTH EYES
PARALYZED EYE
MOBILE V EYE
S1 N = 57
S2 N = 63
S3 N = 64
S4 N = 62

Since shifting from sedation to anesthesia results in a complete recovery from the effects of chronic monocular paralysis (i.e., restoration in the X/Y ratio to normal values), data obtained from these same animals in such a manner prior to the removal of V was used as a referent to assess the extent of recovery which resulted following the removal of V. As indicated in Figure 3, the percentage of X and Y cells recorded under sedated recording conditions was 21.4% and 75.0% respectively, compared to values recorded in virtually the same electrode track but during anesthesia of 69.7% for X cells and 30.3% for Y cells. Shifting from sedation to anesthesia produced a 225.7% change (increase) in the encounter rate for X cells and a 59.6% change (decrease) in that for Y cells. Similarly, relative to preoperative measures removing proprioceptive output from the mobile eye produced an average increase of 222.0% for X cells and an average decrease of 59.5% for Y cells. Based on the Wilcoxon matched-pairs signed-ranks test the recovery observed following the removal of proprioceptive output did not differ significantly from the recovery observed by shifting from sedation to anesthesia. Thus it appears that the X/Y ratio was fully restored once proprioceptive output from the mobile eye was removed.

In conclusion, the removal of proprioceptive signals coming from the mobile eye resulted in an immediate and apparently permanent restoration in the encounter rate for X and Y cells in all principal layers of the LGN, whether the extraocular muscles of the innervating eye were able to provide proprioceptive signals or not.

The removal of V from the paralyzed eye of chronically paralyzed cats. Figure 5 presents the relative percentages of X and Y cells

Figure 5. The relative percentages of X and Y cells recorded from four chronically paralyzed animals before and after the removal of proprioceptive output (V) from the paralyzed eye. The ordinate displays the relative percentages of X cells (top) and Y cells (bottom) encountered in complete penetrations made through the right or left LGN layers A and A1. The left hand panel presents data obtained prior to the removal of V. The stipled bars present the relative percentages of X and Y cells encountered in A and A1 collectively, for sedated (S) and anesthetized (A) pairs of successive electrode penetrations (pass-pairs). The dark and light bars present the relative percentages of cells encountered under sedated recording conditions with the dark bars representing LGN layers innervated by the paralyzed eye, and the light bars representing LGN layers innervated by the mobile eye. The numbers above each bar indicate absolute cell frequencies. The right hand panel presents data obtained from these same animals at 0-5 hrs, 5-10 hrs, 20-25 hrs, and 25-30 hrs after proprioceptive deafferentation.


LGN A&A1
CHRONIC MP
BOTH EYES
PARALYZED-V EYE
MOBILE EYE
PERCENT X-CELLS
PERCENT Y-CELLS
100
90
80
70
60
50
40
30
20
10
0
10
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40
50
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80
90
100
33
23
25
20
27
16
30
15
19
9
22
22
S A
PASS PAIR
PRE-OP
0-5
5-10
20-25
25-30
TIME (HOURS)

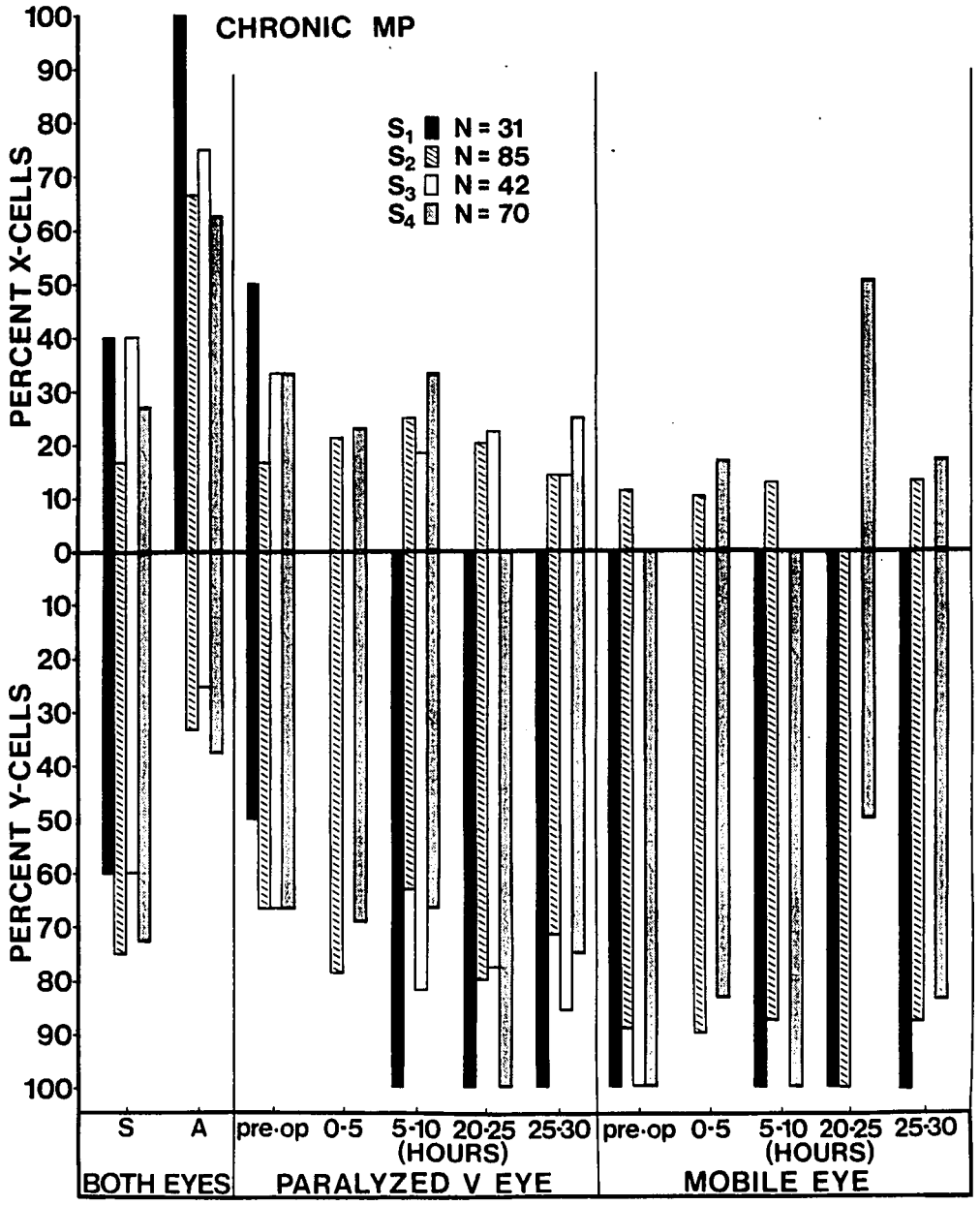
recorded from four chronically monocularly paralyzed cats prior to and after the removal of proprioceptive afferents from the paralyzed eye. For layers innervated by the paralyzed eye the percentage of X cells recorded before the removal of V was 32.0%, compared to postoperative values of 22.2% at 0-5 hrs, 20.0% at 5-10 hrs, 15.8% at 20-25 hrs, and 13.6% at 25-30 hrs. The percentage of Y cells recorded before the removal of V was 64.0% compared to postoperative values of 74.1% at 0-5 hrs, 76.7% at 5-10 hrs, 84.2% at 20-25 hrs and 81.8% at 25-30 hrs. There were no significant differences between values recorded before and at any time after the removal of V from the paralyzed eye.

For layers innervated by the mobile eye the percentage of X cells recorded before the removal of V was 5.0% compared to values of 12.5% at 0-5 hrs, 6.7% at 5-10 hrs, 11.1% at 20-25 hrs, and 13.6% at 25-30 hrs. The percentage of Y cells recorded before the removal of V was 95.0%, compared to postoperative values of 87.5% at 0-5 hrs, 93.3% at 5-10 hrs, 88.9% at 20-25 hrs and 86.4% at 25-30 hrs. For cells innervated by the mobile eye, there were also no significant differences between values recorded before and at any time after the removal of V.

Individual data displayed in Figure 6 indicated that each of the four cats tested showed virtually no sign of change at any time after the removal of V. As can be seen, individual encounter rates, which were based on cell frequencies ranging from 3-14, were able to provide a relatively reliable estimate of cell encounter rates.

Although no recovery was apparent following the removal of V, values obtained preoperatively demonstrated that shifting from sedation to anesthesia results in an immediate recovery from the effects of

Figure 6. Relative percentages of X and Y cells displayed individually for four chronically paralyzed animals before and after the removal of proprioceptive output (V) from the paralyzed eye. Relative precentages for X and Y cells are presented for each of the four animals tested, first, for sedated (S) and anesthetized (A) pairs of successive penetrations which were obtained prior to the removal of V, and then separately for layers innervated by the paralyzed eye and for layers innervated by the mobile eye, before (pre-op) and at 0-5 hrs, 5-10 hrs 20-25 hrs, and 25-30 hrs after the removal of V.


CHRONIC MP
S_1 N = 31
S_2 N = 85
S_3 N = 42
S_4 N = 70
PERCENT X-CELLS
PERCENT Y-CELLS
100
90
80
70
60
50
40
30
20
10
0
10
20
30
40
50
60
70
80
90
100
S
A
pre-op
0-5
5-10
20-25
25-30
(HOURS)
pre-op
0-5
5-10
20-25
25-30
(HOURS)
BOTH EYES
PARALYZED V EYE
MOBILE EYE

chronic monocular paralysis. As indicated in Figure 5 the percentage of X and Y cells recorded under sedation was 27.3% and 69.7% respectively, compared to values recorded in virtually the same electrode track but under anesthesia of 74.0% for X cells and 26.0% for Y cells. Shifting from sedation to anesthesia resulted in a 153.4% increase for X cells and a 59.6% decrease for Y cells. In contrast, removing proprioceptive afferents from the paralyzed eye did not result in any detectable changes in any of the four cats tested.

Thus, the removal of proprioceptive afferents from an orbit containing a chronically paralyzed eye had no detectable effect on the recordability of LGN cells. From a methodological standpoint these results are important, because they rule out the possibility that surgical trauma or residual anesthesia contributed to the changes observed when proprioceptive output was removed from the mobile eye.

The removal of II+V from the mobile eye of acutely paralyzed cats.

Figure 7 presents the relative percentages of X and Y cells recorded from four 4 acutely monocularly paralyzed cats after the combined removal of retinal and proprioceptive output from the mobile eye. Figure 8 presents individual data for these animals. Since acute monocular paralysis represents the normal referent (Salinger et al., 1977; Garraghty et al., 1982) this condition helped to ascertain whether deafferentation by cranial nerve section has a nonspecific effect on the excitability of LGN cells. These data have important implications for intrepreting the effects observed following deafferentation in chronically paralyzed animals. Further, it was

Figure 7. The relative percentages of X and Y cells recorded from four acutely paralyzed animals before and after the removal of retinal and proprioceptive output (II+V) from the mobile eye. The ordinate displays the relative percentages of X cells (top) and Y cells (bottom) encountered in complete penetrations made through the right or left LGN layers A and A1. The left hand panel presents data obtained prior to the removal of II+V. The stipled bars present the relative percentages of X and Y cells encountered in A and A1 collectively, for sedated (S) and anesthetized (A) pairs of successive electrode penetrations (pass-pairs). The dark and light bars present the relative percentages of cells encountered under sedated recording conditions with the dark bars representing LGN layers innervated by the paralyzed eye, and the light bars representing LGN layers innervated by the mobile eye. The numbers above each bar indicate absolute cell frequencies. The right hand panel presents data obtained from these same animals at 0-5 hrs, 5-10 hrs, 20-25 hrs, and 25-30 hrs after retinal and proprioceptive deafferentation.

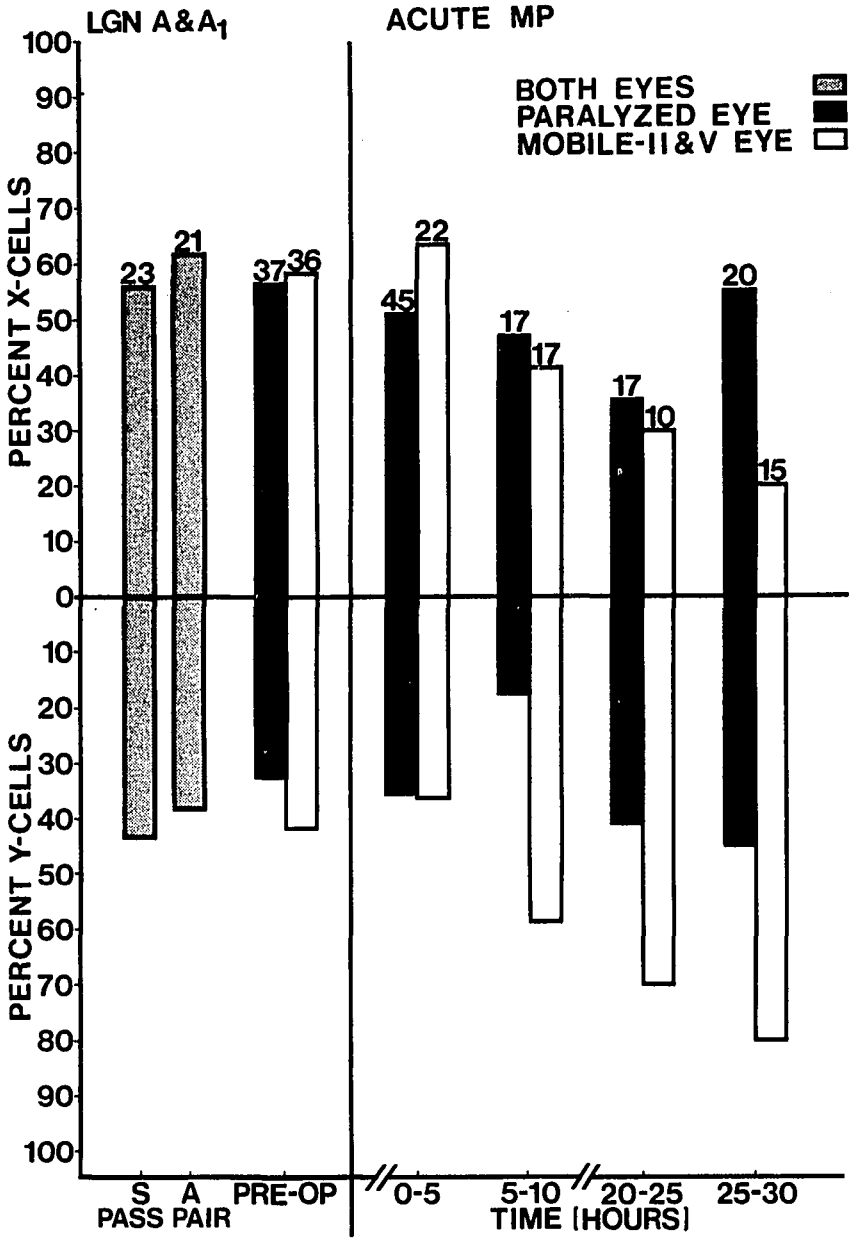
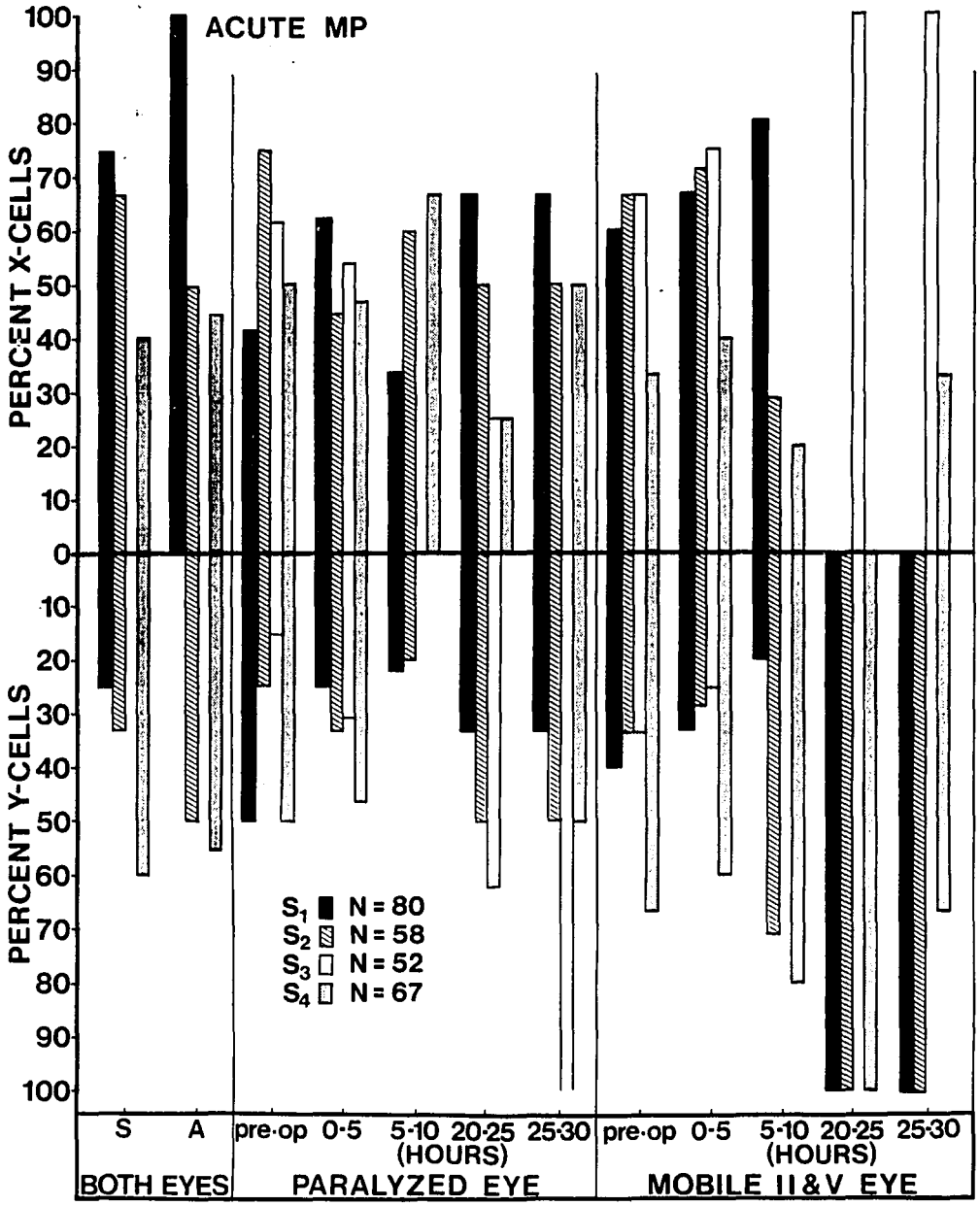

LGN A&A1
ACUTE MP
BOTH EYES
PARALYZED EYE
MOBILE-II&V EYE
PERCENT X-CELLS
PERCENT Y-CELLS
100
90
80
70
60
50
40
30
20
10
0
10
20
30
40
50
60
70
80
90
100
23
21
37
36
45
22
17
17
17
10
20
15
S A
PASS PAIR
PRE-OP
0-5
5-10
20-25
25-30
TIME (HOURS)

Figure 8. Relative percentages of X and Y cells displayed individually for four acutely paralyzed animals before and after the removal of retinal and proprioceptive output (II+V) from the mobile eye. Relative precentages for X and Y cells are presented for each of the four animals tested, first, for sedated (S) and anesthetized (A) pairs of successive penetrations which were obtained prior to the removal of II+V, and then separately for layers innervated by the paralyzed eye and for layers innervated by the mobile eye, before (pre-op) and at 0-5 hrs, 5-10 hrs 20-25 hrs, and 25-30 hrs after the removal of II+V.


ACUTE MP
PERCENT X-CELLS
PERCENT Y-CELLS
100
90
80
70
60
50
40
30
20
10
0
10
20
30
40
50
60
70
80
90
100
S1 N = 80
S2 N = 58
S3 N = 52
S4 N = 67
S
A
pre-op
0-5
5-10
20-25
25-30
(HOURS)
pre-op
0-5
5-10
20-25
25-30
(HOURS)
BOTH EYES
PARALYZED EYE
MOBILE II & V EYE

necessary to determine the pattern of such effects; namely, are such effects interocular in nature, or are they confined only to LGN cells whose afferents were removed.

Data collected in layers innervated by the paralyzed eye whose retinal and proprioceptive afferents remained intact would determine whether removing output from one eye has an effect on the recordability of cells innervated by the other eye (i.e., interocular effects). The percentage of X cells recorded in layers innervated by paralyzed eye before the combined removal of II+V was 56.8%, compared to postoperative values of 51.1% at 0-5 hrs, 47.1% at 5-10 hrs, 35.3% at 20-25 hrs, and 55.0% at 25-30 hrs. The percentage of Y cells recorded preoperatively was 32.4%, compared to postoperative values of 35.6 at 0-5 hrs, 17.6 at 5-10 hrs, 41.2 at 20-25 hrs, and 45.0% at 25-30 hrs. The percentage of X cells did not change significantly following the removal of II+V. The percentage of Y cells, however, did change significantly over time ($p<.01$), but as simple comparisons revealed, it was due to a significant decline recorded only at 0-5 hrs ($p<.01$), with values recorded between 10 and 30 hrs resembling values obtained preoperatively. With the exception at 0-5 hrs for Y cells, the encounter rates from layers innervated by an acutely paralyzed eye remained relatively stable following deafferentation of the other eye. Thus, these results rule out the possibility that factors associated with cranial nerve section (i.e., surgical trauma or deafferentation of LGN cells from adjacent laminae) had an interocularly or systemically mediated effect that could potentially influence the recordability of LGN cells.

Although for chronic monocular paralysis shifting from sedation to

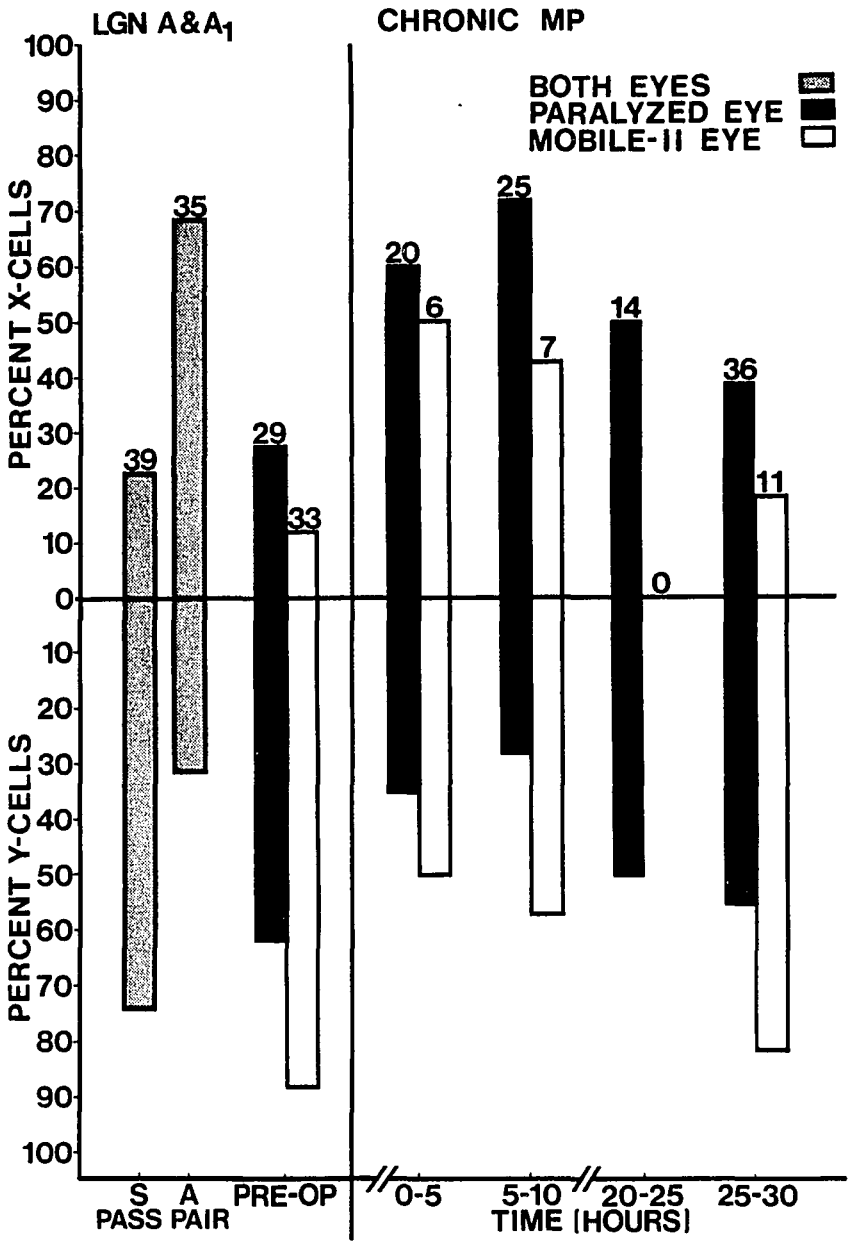
anesthesia has a powerful effect on the recordability of LGN cells, the same manipulation does not have a comparable effect for acute monocular paralysis (Garraghty et al., 1982; Schroeder et al., 1984). As indicated in Figure 7 the percentage of X and Y cells under sedation was 56.5% and 43.5%, respectively, compared to values recorded in virtually the same electrode track but under anesthesia of 61.9% for X cells and 38.1% for Y cells. As can be seen, shifting from sedation to anesthesia had virtually no effect encounter rates for LGN cells. These data are useful, however, since they represent the degree of variability inherent in the present sampling procedures.

Data collected from layers innervated by the mobile eye, which of course contain deafferented LGN cells, were used to help ascertain whether LGN cells, although not injured by cranial nerve section, are directly affected by deafferentation. For layers innervated by the mobile eye the percentage of X cells recorded before the combined removal of II+V was 58.3%, compared to postoperative values of 63.6% at 0-5 hrs, 41.2% at 5-10 hrs, 30.0% at 20-25 hrs, and 20.0% at 25-30 hrs. The percentage of Y cells recorded preoperatively was 41.7%, compared to postoperative values of 36.4% at 0-5 hrs, 58.8% at 5-10 hrs, 70.0% at 20-25 hrs, and 80.0% at 25-30 hrs. There was no significant difference between values recorded before and 0-5 hrs after the removal of II+V. Between 5-10 and 25-30 hrs there was a progressive and significant decline in the encounter rate for X cells ($p<.01$) and a corresponding decrease in that for Y cells ($p<.01$), relative to values obtained at 0-5 hrs. Since the removal of V alone from the paralyzed eye had no detectable effect on LGN physiology (see above), the changes observed

here in layers innervated by deafferented eye, most likely are attributable to the visual deafferentation of LGN cells. Thus, these data suggest that visual deafferentation of LGN cells has a rapid and powerful effect upon the recordability of LGN cells. The changes observed after five hrs are likely attributable to factors such as a deterioration of signal transmission through axotomized retinal ganglion cell axons which project directly on to LGN neurons (Eysel, Grusser, &, Saavedra, 1974). Thus for chronic conditions in which II was sectioned alone or in combination with V, changes in the encounter rate for LGN cells recorded five or more hours after surgery, are likely to be contaminated by consequences of visual deafferentation per se.

The removal of II from the mobile eye of chronically paralyzed cats. Figure 9 presents the relative percentages of X and Y cells recorded from four chronically monocularly paralyzed cats prior to and after the removal of retinal output (II) from the mobile eye. For layers innervated by the paralyzed eye the percentage of X cells recorded before the removal of II was 27.6%, compared to postoperative values of 60.0% at 0-5 hrs, 72.0% at 5 10 hrs, 50.0% at 20-25 hrs, and 38.9% at 25-30 hrs. The percentage of Y cells recorded in layers innervated by the paralyzed eye before the removal of II was 62.1%, compared to postoperative values of 35.0% at 0-5 hrs, 28.0% at 5-10 hrs, 38.9% at 25-30 hrs. Significant changes in the encounter rate for X cells ($p<.01$) and Y cells ($p<.01$) occurred at one or more times of recording (simple main effect of time). Simple comparisons made between values recorded before and at 0-5 hrs and 5-10 hrs after the removal of II indicated that these changes were the result of a significant

Figure 9. The relative percentages of X and Y cells recorded from four chronically paralyzed animals before and after the removal of retinal output (II) from the mobile eye. The ordinate displays the relative percentages of X cells (top) and Y cells (bottom) encountered in complete penetrations made through the right or left LGN layers A and A1. The left hand panel presents data obtained prior to the removal of II. The stipled bars present the relative percentages of X and Y cells encountered in A and A1 collectively, for sedated (S) and anesthetized (A) pairs of successive penetrations (pass-pairs). The dark and light bars present the relative percentages of cells encountered under sedated recording conditions with the dark bars representing LGN layers innervated by the paralyzed eye, and the light bars representing LGN layers innervated by the mobile eye. The numbers above each bar indicate absolute cell frequencies. The right hand panel presents data obtained from these same animals at 0-5 hrs, 5-10 hrs, 20-25 hrs, and 25-30 hrs after deafferentation.


LGN A&A1
CHRONIC MP
BOTH EYES
PARALYZED EYE
MOBILE-II EYE
PERCENT X-CELLS
PERCENT Y-CELLS
100
90
80
70
60
50
40
30
20
10
0
10
20
30
40
50
60
70
80
90
100
39
35
29
33
20
6
25
7
14
0
36
11
S
A
PRE-OP
PASS PAIR
0-5
5-10
20-25
25-30
TIME (HOURS)

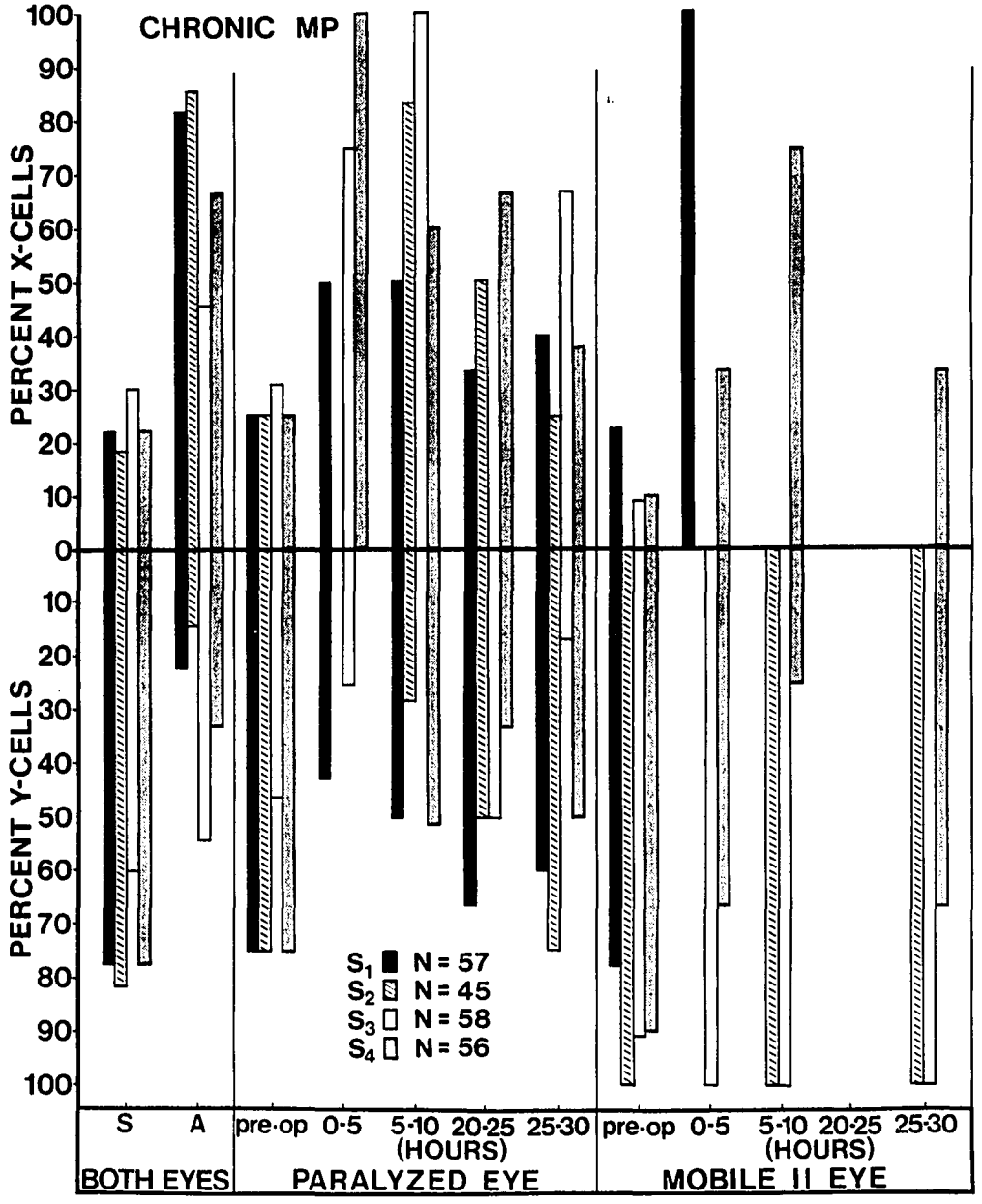
increase in the encounter rate for X cells ($p<.01$) and a corresponding decrease in that for Y cells ($p<.01$), changes which reflect a restoration of the X/Y ratio to normal values. Further, there was no difference between values recorded at 5-10 hrs and 20-25 hrs, but significant differences were obtained between 5-10 hrs and 25-30 hrs ($p<.01$). This pattern suggests that the duration of recovery was limited to 25 hrs. Individual data (layers innervated by the paralyzed eye) displayed in Figure 10 indicated that each of the four cats tested showed a recovery which lasted 25 hrs, and that virtually all values obtained thereafter reflected a clear absence of recovery. Thus, these encounter rates, which individually, were based on cell frequencies ranging from 4-14, were able to provide a relatively accurate and reliable estimate of LGN physiology.

Although excluded from the analysis, data collected beyond 30 hrs at 30-35 hrs (see Appendix B) resembled values recorded before and 25-30 hrs after the removal of II and apparently confirm that the recovery which was observed after the removal of II was limited to 25 hrs.

For layers innervated by the mobile eye, the percentage of X cells recorded before the removal of II was 12.1%, compared to a postoperative value of 50% at 0-5 hrs. The percentage of Y cells recorded before the removal of II was 87.9% compared to 50% at 0-5 hrs. Simple comparisons made between values recorded before and 0-5 hrs after the removal of II indicated a significant increase in the encounter rate for X cells and a corresponding decrease in that for Y cells ($p<.01$).

Compared to 0-5 hrs, values recorded between 5-10 hrs and 25-30 hrs and seem to reflect a progressive decline in the encounter rate for X

Figure 10. Relative percentages of X and Y cells displayed individually for four chronically paralyzed animals before and after the removal of retinal output (II) from the mobile eye. Relative precentages for X and Y cells are presented for each of the four animals tested, first, for sedated (S) and anesthetized (A) pairs of successive penetrations which were obtained prior to the removal of II, and then separately for layers innervated by the paralyzed eye and for layers innervated by the mobile eye, before (pre-op) and at 0-5 hrs, 5-10 hrs 20-25 hrs, and 25-30 hrs after the removal of II.


CHRONIC MP
PERCENT X-CELLS
PERCENT Y-CELLS
100
90
80
70
60
50
40
30
20
10
0
10
20
30
40
50
60
70
80
90
100
S
A
pre-op
0-5
5-10
20-25
25-30
(HOURS)
pre-op
0-5
5-10
20-25
25-30
(HOURS)
BOTH EYES
PARALYZED EYE
MOBILE II EYE
S1 N = 57
S2 N = 45
S3 N = 58
S4 N = 56

cells (42.9% at 5-10 hrs, 18.2% at 25-30 hrs) and a corresponding increase in that for Y cells (57.1% at 5-10 hrs, 81.8% at 25-30 hrs). The timing and pattern of such a decline corresponded to that observed following the removal of II+V in acutely paralyzed animals, thus making it very likely that such changes were brought about by the deafferentation of LGN cells. For this reason, it was not possible (or appropriate) to assess the presence or absence of a recovery at times greater than 5 hrs since such measures could be confounded by direct consequences of deafferentation.

Inspection of the individual data (layers innervated by the mobile eye) displayed in Figure 10 seem to indicate that values obtained at 0-5 hrs are consistent across each animal but that values obtained beyond 5 hrs became highly variable with respect to each other. This may in part be due to exceptionally low cell counts (range of 0-6) recorded at these times.

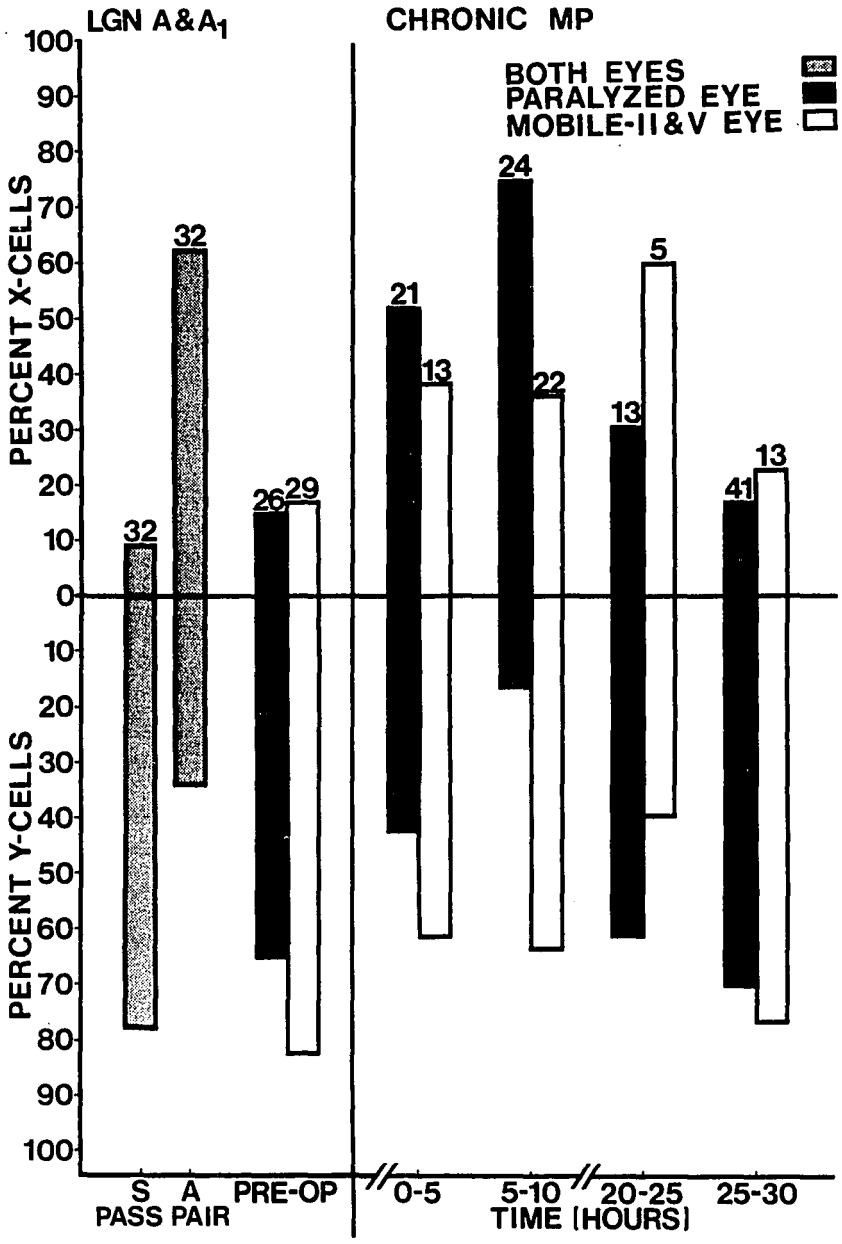
The extent to which such a recovery produced by the removal of II could be judged as complete was examined, by using as a referent, the change produced by shifting from sedation to anesthesia preoperatively. As displayed in Figure 9 the percentage of X and Y cells recorded under sedation was 23.0% and 74.5% respectively, compared to values of 68.6% for X cells and 31.4% for Y cells, under anesthesia. In paired penetrations, shifting from sedation to anesthesia resulted in a 198.2% increase in the encounter rate for X cells and a 57.8% decrease in that for Y cells. Similarly, removing retinal output from the mobile eye resulted in an average increase of 190.1% for X cells and an average decrease of 57.2% for Y cells. The recovery observed following the

removal of II was not significantly different (Wilcoxon) from that observed preoperatively by shifting from sedation to anesthesia. Thus, it appears that the recovery observed between 0-25 hrs represents a complete recovery from the effects of chronic monocular paralysis.

In conclusion, for layers innervated by the paralyzed eye the removal of retinal output from the mobile eye resulted in an immediate recovery which lasted 25 hrs. Similarly, for layers innervated by the mobile eye an immediate recovery was detected, but because deafferentation per se produces a change in X/Y encounter rates, it was not possible to assess whether the duration of such a recovery lasted beyond 5 hrs.

The removal of II+V from the mobile eye of chronically paralyzed cats. Figure 11 presents the relative percentages of X and Y cells recorded from four chronically monocularly paralyzed cats prior to and after the combined removal of retinal and proprioceptive (II+V) output from the mobile eye. For layers innervated by the paralyzed eye the percentage of X cells recorded before the combined removal of II+V was 15.4%, compared to values of 52.4% at 0-5 hrs, 75.0% at 5-10 hrs, 30.8% at 20-25 hrs, and 17.1% at 25-30 hrs. The percentage of Y cells recorded prior to the removal of II+V was 65.4%, compared to postoperative values of 42.9% at 0-5 hrs, 16.7% at 5-10 hrs, 61.5% at 20-25 hrs, and 70.7% at 25-30 hrs. Significant changes for X cells ($p<.01$) and Y cells ($p<.01$) occurred at one or more times of recording (simple main effect of time). Simple comparisons between values recorded before and at 0-5 hrs and 5-10 hrs after the removal of II+V indicated that such changes were the result of a significant increase in

Figure 11. The relative percentages of X and Y cells recorded from four chronically paralyzed animals before and after the removal of retinal and proprioceptive output (II+V) from the mobile eye. The ordinate displays the relative percentages of X cells (top) and Y cells (bottom) encountered in complete penetrations made through the right or left LGN layers A and A1. The left hand panel presents data obtained prior to the removal of II+V. The stipled bars present the relative percentages of X and Y cells encountered in A and A1 collectively, for sedated (S) and anesthetized (A) pairs of successive electrode penetrations (pass-pairs). The dark and light bars present the relative percentages of cells encountered under sedated recording conditions with the dark bars representing LGN layers innervated by the paralyzed eye, and the light bars representing LGN layers innervated by the mobile eye. The numbers above each bar indicate absolute cell frequencies. The right hand panel presents data obtained from these same animals at 0-5 hrs, 5-10 hrs, 20-25 hrs, and 25-30 hrs after deafferentation.


LGN A&A1
CHRONIC MP
BOTH EYES
PARALYZED EYE
MOBILE-II&V EYE
PERCENT X-CELLS
PERCENT Y-CELLS
100
90
80
70
60
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40
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20
10
0
10
20
30
40
50
60
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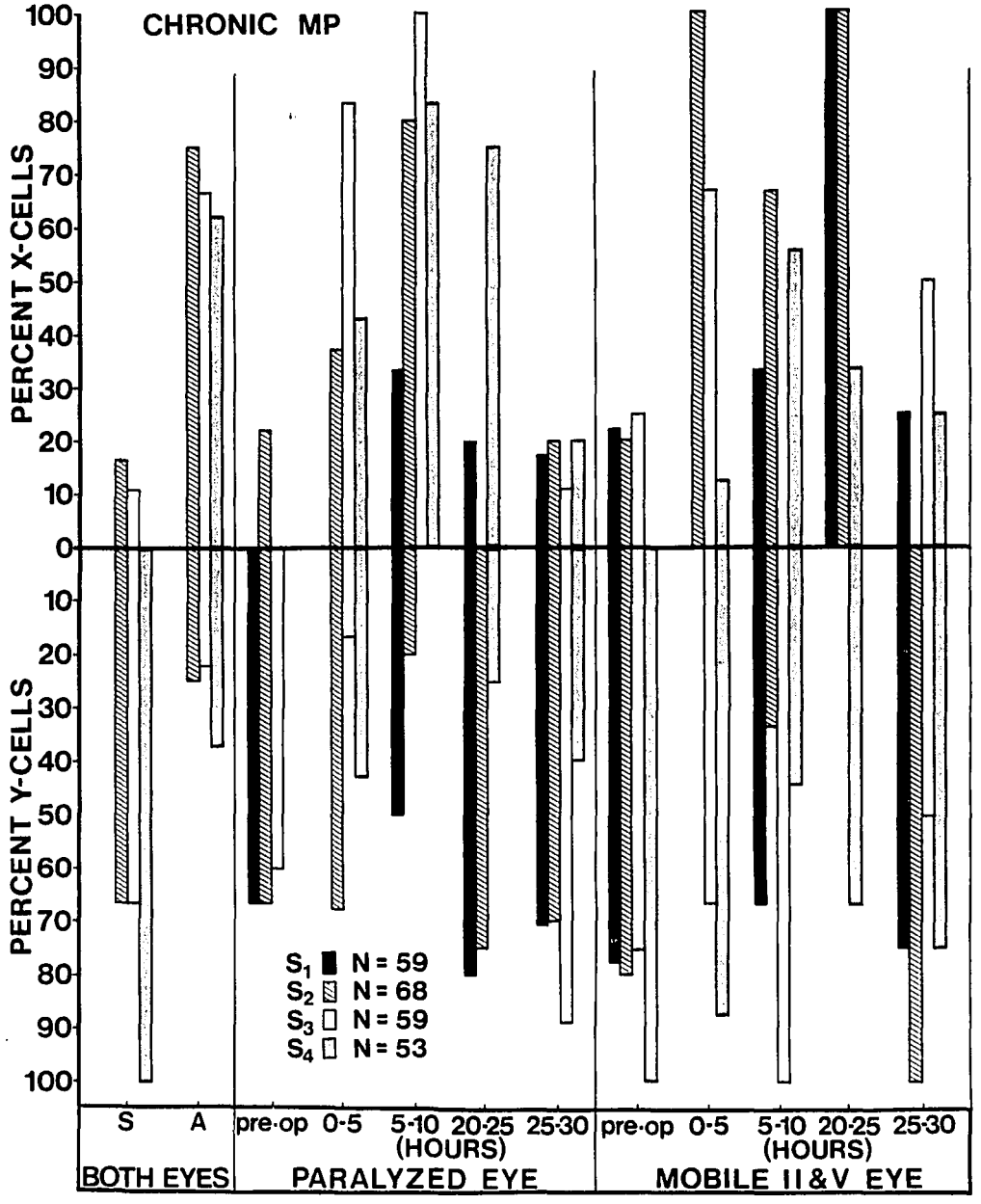
80
90
100
32
32
26
29
21
13
24
22
13
5
41
13
S
A
PRE-OP
0-5
5-10
20-25
25-30
PASS PAIR
TIME (HOURS)

the encounter rate for X cells ($p<.01$) and a corresponding decrease for Y cells, suggesting that the combined removal of II+V resulted in an immediate recovery which lasted 10 hrs. Values recorded at 20-25 hrs and at 25-30 hrs, however, differed (decrease in X and increase in Y) significantly from values recorded at 5-10 hrs ($p<.01$). The decline in the encounter rate for X cells and coresponding increase in that for Y cells starting at 20-25 hrs suggests that the duration of recovery was limited to no more than 10 hrs. Individual data (layers innervated by the paralyzed eye) displayed in Figure 12 indicated that each of the four cats tested had undergone an immediate recovery which lasted 10 hrs and virtually all values recorded after 20 hrs reflected a clear absence of a recovery. Encounter rates for individuals were based on cell frequencies ranging from 3-18, and although smaller than the frequencies associated with the grouped encounter rates, they seem to provide a relatively reliable estimate of LGN physiology. Further, data obtained at 30-35 hrs, although excluded from the analysis, resembled values recorded postoperatively at 20-25 hrs and 30-35 hrs.

For layers innervated by the mobile eye the percentage of X cells recorded before the combined removal of II+V was 17.2%, compared to postoperative values of 38.5% at 0-5 hrs. while the percentage of Y cells recorded before the removal of II+V was 82.8%, compared to postoperative values of 61.5% at 0-5 hrs. Simple comparisons made between values recorded before and 0-5 hrs after the removal of II+V indicated a significant increase in X cells ($p<.01$) and corresponding decrease for Y cells ($p<.01$).

Values recorded beyond 5 hrs seem to indicate overall, a

Figure 12. Relative percentages of X and Y cells displayed individually for 4 chronically paralyzed animals before and after the removal of retinal and proprioceptive output (II+V) from the mobile eye. Relative precentages for X and Y cells are presented for each of the four animals tested, first, for sedated (S) and anesthetized (A) pairs of successive penetrations which were obtained prior to the removal of II+V, and then separately for layers innervated by the paralyzed eye and for layers innervated by the mobile eye, before (pre-op) and at 0-5 hrs, 5-10 hrs 20-25 hrs and 25-30 hrs after the removal of II+V.


CHRONIC MP
PERCENT X-CELLS
PERCENT Y-CELLS
100
90
80
70
60
50
40
30
20
10
0
10
20
30
40
50
60
70
80
90
100
S1 N = 59
S2 N = 68
S3 N = 59
S4 N = 53
S
A
pre-op
0-5
5-10
20-25
25-30
(HOURS)
pre-op
0-5
5-10
20-25
25-30
(HOURS)
BOTH EYES
PARALYZED EYE
MOBILE II&V EYE

progressive decline in the encounter rate for X cells (36.4% at 5-10 hrs, 60.0% at 20-25 hrs, 23.0% at 25-30 hrs) and a corresponding increase for Y cells (63.3% at 5-10 hrs, 40.0% at 20-25 hrs, and 76.9% at 25-30 hrs). The timing and pattern of such changes corresponds to that observed following the removal of II+V in acute animals and II in chronic animals, and again, may reflect the effects of deafferentation per se.

The extent to which the recovery associated with the combined removal of II+V could be judged as complete was examined by using data collected preoperatively from sedated and anesthetized pairs. As indicated in Figure 12, the percentage of X and Y cells recorded from these animals under sedation was 9.4% and 78.1% respectively, compared to values obtained in virtually the same electrode track but during anesthesia of 62.5% for X cells and 34.4% for Y cells. Shifting from sedation to anesthesia resulted in a 564.8% increase in the encounter rate for X cells and a 56.0% decrease in that for Y cells. Similarly, the combined removal of II+V resulted in an average increase of 455.0% for X cells and a decrease of 44.9% for Y cells. The recovery observed following the removal of II+V was not significantly different (Wilcoxon) from that observed preoperatively by anesthesia pass pairs. Thus the removal of II+V produced a complete, albeit transient recovery of the X/Y ratio to normal values.

In conclusion, for layers innervated by the paralyzed eye, the combined removal of retinal and proprioceptive ouput from one eye resulted in an immediate but transient recovery lasting no more than 10 hrs. For layers innervated by the mobile eye, the combined removal of

II+V resulted in an immediate recovery, but because of the effects associated with visual deafferentation per se it was not possible to assess whether the duration of such a recovery lasted beyond 5 hrs.

CHAPTER IV

DISCUSSION

The present experiment examined the physiological effects associated with the removal of proprioceptive signals from extraocular muscles and/or visual signals from one eye in the lateral geniculate nucleus (LGN) of monocularly paralyzed cats.

The Role of Orbital Proprioceptive Signals in Maintaining the Effects of Chronic Monocular Paralysis

The removal of proprioceptive afferents (V) from a chronically paralyzed eye. In each of the four chronically paralyzed cats tested, the removal of proprioceptive afferents innervating extraocular muscles of a paralyzed eye had no detectable effect on the recordability of LGN cells. The relative encounter rates for X and Y cells obtained from all principal layers of both LGNs did not differ from values obtained before the removal of V. Because these animals had been monocularly paralyzed for two or more weeks prior to the removal of V, the X/Y ratio reflected a relative reduction in the encounter rate for X cells and a relative increase for Y cells. One might be tempted to conclude that proprioceptive signals play no role in maintaining the physiologic effects associated chronic monocular paralysis. Moreover, at first glance, these results also suggest that LGN cells as a whole are not sensitive to orbital proprioceptive signals. These conclusions seem

unlikely however, for two reasons. First, proprioceptive signals arising from extraocular muscles have been shown to exert a powerful effect on LGN activity (Donaldson & Dixon, 1980), and second proprioceptive asymmetries produced by paralyzing one eye have been shown to contribute substantially to the shift in X/Y ratio induced by chronic monocular paralysis (Salinger, Garraghty, & Schwartz, 1980). Taken together, these studies indicate that the LGN is in fact sensitive to orbital proprioceptive signals and, that such signals are critical in shifting the X/Y ratio during chronic monocular paralysis. Therefore, the question which arises from the present experiment in which proprioceptive output was removed from the paralyzed eye is whether the LGN is insensitive to proprioceptive signals arising from an orbit which contains a paralyzed eye rather than a mobile eye. In the context of monocular paralysis, if the LGN is not sensitive to orbital proprioceptive signals arising from a paralyzed eye, it would be very unlikely that removing proprioceptive afferents from such an eye would have an effect on unit excitability.

What are the signals which arise from a paralyzed eye and do they differ from signals which originate from a mobile eye? In a normal moving eye, two types of responses have been recorded from proprioceptors in extraocular muscles (EOMs) or from their respective afferent fibers: "dynamic" signals which correspond to muscle stretch (whether it be muscle length or actual velocity), and static signals which, in the absence of muscle stretch, correspond to muscle length and therefore eye position (Bach-Y Rita & Ito, 1966a, 1966b; see Batini, 1979). In the paralyzed eye, however, since the eye muscles are

permanently immobilized by prior transection of oculomotor nerves III, IV, VI, it is unlikely that dynamic proprioceptive signals conveying orbital movement are present. However, a static signal which does not depend on transient muscle stretch but instead is related to orbital position could conceivably persist in an orbit containing a paralyzed eye.

Are LGN cells sensitive to static signalling? In the LGN of the cat, Donaldson and Dixon (1980) have recorded phasic excitatory unit responses to EOM stretch but failed to detect any tonic unit activity which could be correlated with orbital position per se. It appears that LGN cells seem to lack a sensitivity to orbital position information. Although static eye position signals from a paralyzed eye could conceivably persist and thus be eliminated following the section of V, there is no available experimental evidence to suggest that the LGN should be responsive to such signals, and therefore to manipulations which would eliminate them. By this reasoning, the failure to detect changes following the removal of V from a paralyzed eye may not necessarily mean that the LGN is insensitive to proprioceptive signals but only that it is insensitive to static signals, such as those which may arise from a paralyzed eye. If this line of reasoning is correct, removing proprioceptive afferents from a mobile eye rather than a paralyzed eye may produce a profound effect on LGN physiology.

<u>The removal of proprioceptive afferents from the mobile eye of chronically paralyzed cats</u>. In each of the four chronically paralyzed cats tested the removal of proprioceptive output from the mobile eye resulted in an immediate and relatively permanent shift in X/Y encounter

rates in a direction which reflected a complete recovery from the effects of chronic monocular paralysis. Further, this recovery was observed in all principal layers of both LGNs whether the proprioceptive afferents from the visually innervating eye were intact or not. The failure to detect similar changes following the section of V on the side of the paralyzed eye excludes the possibility that these changes, occurring once proprioceptive afferents were removed from the mobile eye, might be due to surgical trauma or residual effects from surgical anesthesia. For the same reason it is also unlikely that sensory and/or motoric innervation of the orbit or its surround (e.g., the parts of the eye, nasal mucosa, frontal sinus, external nose, upper eyelid, forehead and scalp) which is also carried along the ophthalmic branch of the trigeminal nerve (see Gardener, Gray, & O'Rahilly, 1975) contributed to the changes in X/Y encounter rates once V from the mobile eye was sectioned. It is conceivable that sectioning V from the mobile eye, in addition to eliminating proprioceptive signals, removed tactile signals which may arise from movements of the eye rubbing against the eyelid. While this possibility cannot be ruled out, it seems unlikely that the elimination of such signals would be responsible for the shift in recordability of visual cells. It seems more likely the case that the removal of dynamic proprioceptive signals originating from extraocular muscles of the mobile eye, are responsible for such changes. Interpreted in this fashion, these results complement the findings obtained from the lid suture experiments (Salinger, Garraghty, & Schwartz, 1980), which demonstrated that proprioceptive asymmetries were critical in generating the effects of monocular paralysis. Finally,

this interpretation requires that orbital proprioceptive signals reach the LGN.

Orbital proprioceptive reponses in LGN. Several investigators have shown that extraretinal signals in the form of sensory feedback from EOMs reach a variety of visual and visuomotor structures. For example, unit responses to EOM stretch or to electrical stimulation of oculomotor nerves have been found in intermediate layers (Rose & Abrahams, 1975) and superficial layers of superior colliculus (Donaldson & Long, 1980), in thalamic nuclei including LGN, medial interlaminar nucleus, and perigeniculate nucleus (Donaldson & Dixon, 1980), and in visual cortical areas including area 17 (Buissert & Maffei, 1977; Ashton, Boddy & Donaldson, 1983, in press) and lateral supersylvian cortex (Donaldson, 1979).

In the LGN a great majority of visually responsive relay cells are known to give phasic excitatory responses to passive displacements of the eye (Donalson & Dixon, 1980). These responses were demonstrated to be truly extraretinal in origin, arising from EOM proprioceptors (see Batini, 1979), since such activity persisted in total darkness, or after the retina was destroyed and the globe collapsed. Although these electrophysiological reports along with the results from the present study require the presence of afferent pathways to LGN from extraocular musculature, neuroanatomical support for a direct pathway to the LGN seems to be lacking. However, a substantial amount of neuroanatomical evidence has accumulated which supports the above electrophysiological studies, suggesting that proprioceptive signals are routed to the LGN indirectly.

Pathways and central projections of extraocular muscle afferents. The extraocular muscles of many vertebrate species contain stretch receptors (Batini, 1979; see Maier, DeSantis, & Eldred, 1974). In the cat, a rich supply of specialized terminals has been identified in extraocular muscles and tendinous attachments (Alvarado-Mallart & Pincon-Reymond, 1979; Cooper & Fillenz, 1955). It is believed that proprioceptive fibers run extraorbitally and enter the brain along the ophthalmic branch of the trigeminal nerve (V) (Batini & Buisseret, 1974; Batini et al., 1975; Buisseret-Delmas, 1976). Recently, first order neurons of proprioceptive afferents have also been identified in the ophthalmic subdivision of the semilunar ganglion of V (Alvarado-Mallart, Batini, Buisseret-Delmas, Gueritand, & Horchelle-Bossavit, 1975; Porter & Spencer, 1982).

The sensory nuclei of the trigeminal nerve consist of three parts, spinal trigeminal nucleus, main sensory nucleus, and mesencephalic sensory nucleus, which together extend through the brainstem from the second cervical segment of the spinal cord and upward through the mesencephalon (Brodal, 1981). Second order neurons of EOM priopriоceptors have been identified in spinal trigeminal nucleus (Manni, Palmieri, & Marini, 1971, 1972, 1974) and mesencephalic nucleus (Alvarado-Mallart, Batini, Buisseret-Delmas, Corvisier, 1975; Alvarado-Mallart, Batini, Buisseret, Gueritand, & Horchelle-Bossavit, 1975; Cooper & Fillenz, 1955). The identification of neurons in mesencephalic nucleus of V however, has since been traced to masticatory muscle proprioceptors and not to EOM proprioceptors (Porter & Spencer, 1982; see also Jerge, 1963).

Neurons of spinal trigeminal nucleus (STN) are known to project to a variety of central structures including mesencephalic reticular formation, ventral posterior medial nuclear complex of thalamus (Torvik, 1956; Smith, 1975), and superior colliculus, (Abrahams & Rose, 1975). Projections from STN to these structures could thus provide a possible neuroanatomical substrate for the relay of EOM signals. Further, in the absence of a direct projection from semilunar ganglion or spinal trigeminal nucleus to the LGN it is conceivable that the well-established ascending connections to LGN from mesencephalic reticular formation (Ahlsen & Lo, 1982; Bowsher, 1970; Hughes & Mullikin, 1984), superior colliculus (Graham, 1977; Harrell, Caldwell & Mize, 1982) and adjacent thalamic nuclei (Jones, 1975; Scheibel & Scheibel, 1966; Szentagothai, 1973) could serve as the route for EOM signals which are recorded in LGN as well as visual cortical areas.

Proprioception and interocular interactions in LGN. In the present experiment, once proprioceptive afferents from the mobile eye were removed, substantial and equivalent shifts in X/Y ratio were recorded in all principal layers of both the right and left LGN. This pattern of results indicates that proprioceptive output from the orbit of one eye can affect the excitability of LGN cells innervated by the other eye. This finding is also consistent with previous results in which EOM signals arising from one eye were found to excite LGN neurons innervated by the other eye; nonetheless, the majority of LGN neurons (72%) found to be reponsive to stretch were innnervated by the eye whose EOMs were stretched (Donaldson & Dixon, 1980). In contrast to the subtle interactions observed by Donaldson and Dixon (1980), the results of the

present study seem to indicate that a substantial proportion of LGN cells were subject to proprioceptively mediated interocular interactions, and that these interactions were of such strength as to modulate the recordability of X and Y cells.

Neural substrate for proprioceptive interocular interactions. It is possible that nonretinal interocular effects in LGN may mediated by connections between LGN, and adjacent thalamic nuclei located in reticular thalamic complex, or by descending connnections from visual cortex to LGN. Donaldson & Dixon (1980) demonstrated that several visually responsive units in the perigeniculate nucleus (PGN), a thin sheet of cells just dorsal to the LGN and belonging to the reticular thalamic complex (Jones, 1975; Scheibel & Scheibel, 1966), gave phasic excitatory reponses when EOMs were stretched. Other studies have shown that the majority of visually responsive units in PGN are sensitive to retinal output from either eye (Dubin & Cleland, 1977; Sanderson, 1971). Anatomically, reciprocal connections between PGN (Ahlsen & Lindstrom, 1978) and LGN (Ahlsen, Lindstrom, & Sybriska, 1978; Freidlander et al., 1979, 1981) are known to exist. These connections have also been thought of as providing the neural basis of visually mediated interocular interactions in LGN (e.g. Singer, 1977), and since both LGN and PGN cells are responsive to proprioceptive signals from either eye, they could also be responsible for mediating proprioceptive interocular interactions in the LGN. It is also quite possible that interocular interactions involving EOM signal transmission may be mediated by corticofugal projections (see Swadlow, 1983) since it appears that binocularly responsive cortical cells receive input from

EOM afferents as well (Buisseret & Maffei, 1977; Ashton et al., 1983, in press).

The Role of Retinal Output in Maintaining the Effects of Chronic Monocular Paralysis

Deafferentation artifacts in the LGN following optic nerve section. To help evaluate the extent to which visual deafferentation itself may alter the X/Y ratio, control experiments were performed on four acutely paralyzed animals (a preparation which exhibits a normal X/Y ratio) in which output from the mobile eye was removed.

For LGN layers containing deafferented cells (i.e., mobile eye layers), these control experiments indicated that deafferentation had no immediate effect on X/Y ratio, but after five hours it resulted in a progressive reduction in the encounter for rate for X cells relative to Y cells. Accompanying the reduction in X cells was a parallel decline in the number of LGN cells encountered per penetration through deafferented layers to a point where virtually no cells could be encountered at all. These results suggest that LGN cells, although not directly injured, are however strongly influenced by the removal of sensory afferents. It is possible that the the above changes recorded in layers which contain deafferented cells mark the onset of transynaptic degenerative effects which are known to occur when LGN cells lose their retinal input (see Cowan, 1970). It has been well recognized that neurons in the LGN of adult cats atrophy several days after their retinal afferents are interrupted (Cook, Walker, & Barr, 1951). More recently, however, ultrastructural changes among retinal geniculate terminals and LGN cells have been noted as early as 24 hours

after visual deafferentation (Eysel, Grusser, & Saaverdra, 1974; Pecci-Saavedra, Vaccarezza, Reader, & Pasqualini, 1970; Vaccarezza, Reader, Pasqualini & Pecci-Saavedra, 1970). Further, well correlated with these degenerative changes in morphology is a progressive deterioration in signal transmission 24-36 hours after deafferentation, and cessation of all synaptic transmission between 48-96 hours (Eysel et al., 1974). During the time prior to complete cessation, the signal transmission through terminals of class II fibers (X cells) is known to deteriorate faster than that through synapses of class I fibers (Y cells). Whether these degenerative changes occur any earlier than 24 hours, or at different rates for X and Y cells remains to be determined. Assuming that encounter rates can be used as a means to assess X/Y cell excitability and synaptic efficiency (Schroeder et al., 1984), it is conceivable that changes in the X/Y ratio could be used as a means to estimate excitability changes that herald the onset of transynaptic degeneration in the LGN. If so, then based on the present control experiments with acute animals, it appears that the deterioration process begins as early as five hours after deafferentation and seems to effect X cells more quickly than Y cells.

It is important to note that the effects of deafferentation per se seemed to be confined to LGN layers innervated by the deafferented eye. For each of the four acutely paralyzed animals, deafferentation had no detectable effect on the X/Y ratio obtained from layers innervated by the paralyzed eye which had not been visually deafferented. In contrast to the pattern of results obtained from layers innervated by the mobile eye (i.e., deafferented laminae), these results obtained from layers

innervated by the paralyzed eye exclude the possibility that visual deafferentation itself has systemic or interocular effects on LGN physiology.

Thus, for normal (acutely paralyzed) animals it appears that visual deafferentation has no detectable effects on cells whose retinal afferents remain intact (paralyzed eye layers), but in layers innervated by deafferented LGN cells (mobile eye layers), after five or more hours deafferentation results in a relatively permanent reduction in X cells and a progressive decline in the number of cells encountered per pass. These effects are most likely due to the deterioration in signal transmission that ensues soon after LGN retinal afferents are removed. The time course for such effects in layers containing deafferented cells (i.e., mobile eye layers) has implications for interpreting effects in corresponding laminae of chronically paralyzed animals, and suggests that it is only possible to interpret the presence or absence of a recovery within the first five hours after deafferentation.

The removal of retinal output from the mobile eye of chronically paralyzed cats. In each of the four chronically paralyzed cats tested, the removal of retinal output from the mobile eye by optic nerve section resulted in an immediate shift in the X/Y ratio, in a direction of a recovery among all principal layers of both LGNs. For layers innervated by the paralyzed eye this change was evident through the first 20 hours, whereas for layers innervated by the mobile eye it was only possible to interpret these changes through the first five hours for reasons described above. However, unlike the permanent recovery observed following the removal of proprioceptive afferents, the recovery

associated with unilateral optic nerve section in layers innervated by the paralyzed eye was transient. There are two possible explanations which could account for the transient modulation of the X/Y ratio produced by unilateral optic nerve section. First, it is conceivable that a nonspecific, but interocular physiologic process induced by the removal of retinal output, and analogous to "spinal shock syndrome" (see Brodal, 1981) led to an eventual collapse of normal X/Y ratios in the LGN, which had been restored by optic nerve section. At first glance, this possibility seems unlikely, since the eventual decline in the X cell encounter rate observed in chronic animals was not apparent in acute counterparts, which in the face of optic nerve section displayed normal, stable encounter rates. This interpretation applies, but only with regard to animals whose physiology had been modified by chronic monocular paralysis. The second possibility is that the sensory modifications associated with monocular paralysis which persisted in the face of optic nerve section may be responsible for the transient modulation of the X/Y ratio following optic nerve section. For example, although retinal output from the mobile eye was removed by optic nerve section, orbital proprioceptive output from the mobile eye carried along V remains unaffected. As a result, abnormal patterns of extraretinally mediated stimulation (i.e., proprioceptive asymmetries) induced by monocular paralysis are still present and may thus have an effect on the duration of recovery associated with optic nerve section. Additionally, there is output from the chronically paralyzed eye, which may in the context of acute deafferentation of the mobile eye, lead to a transient modulation.

At present there is no way to rule out the possibility that a nonspecific physiologic process which is triggered by optic nerve section was responsible for the transient modulation of the X/Y ratio. The possibility that the remaining retinal afferents (from the paralyzed eye) were contributing to this effect was also not explored, since control experiments on acutely paralyzed animals suggest that layers containing deafferented LGN cells are greatly affected by optic nerve section. A bilateral optic nerve section would lead to artifactual changes in encounter rates. Moreover, a bilateral optic nerve section would make it impossible to isolate and classify LGN cells since the isolation and subsequent identification of LGN cells depend largely on the cells response to visual stimulation. Therefore, the remaining possibility to test was whether residual proprioceptive asymmetries were involved.

The removal of visual and proprioceptive output from the mobile eye of a chronically paralyzed cat. In each of the four chronically paralyzed cats tested the combined removal of retinal and proprioceptive output from the mobile eye produced an immediate shift in X/Y ratio in all principal laminae of both LGNs, and as control experiments indicated, these changes reflected a complete recovery from the effects of monocular paralysis. However, it appears that the combined removal of II+V from the mobile eye had a transient effect, similar to that observed following optic nerve section alone. If abornmal patterns of ocular motility were responsible for the short duration in recovery associated with optic nerve section, then the removal of proprioceptive afferents in combination with retinal afferents should have produced a

sustained pattern of recovery. Since this was not the case, it seems unlikely the abnormal patterns of binocular stimulation arising from asymmetries in proprioceptive signalling accounted for the transient recovery pattern observed following optic nerve section alone. Rather it appears that retinal output from the paralyzed eye may have a sustained influence on LGN cell excitability, whose effect in maintaining the shift in X/Y ratio produced by chronic monocular paralysis is only temporarily blunted when retinal output alone or in combination with proprioceptive output from the mobile eye is removed.

Visually mediated interocular interactions in LGN. Despite the transient nature of the effects associated with optic nerve section (either alone or in combination with trigeminal section) it is clear that LGN cells innervated by one eye are extremely sensitive to the removal of output from the other eye. For example, in chronically paralyzed animals, LGN layers which continued to receive direct visual input from one eye (i.e., paralyzed eye), were affected by the removal of retinal output from the other eye.

Although in the cat the great majority of relay cells in the LGN are innervated directly by either one or a few retinal fibers from the same eye (Cleland, Dubin, & Levick, 1971a; Levick, Cleland & Dubin, 1972) it is well known that the activity of these cells can be suppressed by visual stimulation of the other "nondominant" eye (e.g., Rodieck & Dreher, 1979; Sanderson, Bishop, & Darian-Smith, 1971; Singer, 1970; Suzuki & Takahashi, 1970) or by electrical shocks applied to the nondominant optic nerve (e.g., Suzuki & Kato, 1966; Rodieck & Dreher, 1979). Intracellular recordings have also shown that such

inhibitory interocular effects are postsynaptic (Singer, 1970). They seem to depend largely on circuits intrinsic to the LGN and surrounding thalamic nuclei, since such responses are still present after decortication (Sanderson et al., 1971; Singer, 1970). Further, such interlaminar inhibitory circuits act primarily between cells in lamina A and A1 that are in retinotopic register (see Singer, 1977). In general, the inhibition is far stronger for ipsilateral cells than for contralateral cells and is more prevalent among X cells than Y cells (Fukuda & Stone, 1976; Foote et al., 1977; Rodieck & Dreher, 1979). The results from the present experiment complement the above findings by demonstrating that LGN cells are sensitive to the removal of output from the "nondominant eye".

The relative strength of visually mediated interocular interactions in LGN. Although binocular inhibition is present among LGN cells, under conventional recording conditions (anesthesia and systemic paralysis) it is not found consistently in all neurons tested, and when found, the response itself is relatively weak (e.g., Sanderson et al., 1971; Singer, 1970). Further, other investigators have failed to detect strong binocular interactions among LGN cells in recording preparations which involved anesthesia, general paralysis, and unilateral optic nerve section (Eysel et al., 1974; Eysel & Grusser, 1978). This is somewhat surprising since not only the results of this experiment in which output from one eye was removed, but also those of others which involved chronic monocular paralysis (Garraghty et al., 1982) demonstrated that such inhibitory interactions are powerful and selective enough to modulate the X/Y ratio. The contrast between the strength of inhibitory

interocular interactions observed in preparations involving chronic monocularly paralyzed cats and the more subtle interocular effects observed with normal animals under conventional recording conditions, can be traced to two variables. First, the abnormal visual experience produced by two or more weeks of monocular paralysis could serve to enhance interocular interactions in LGN which under normal binocular retinal stimulation are relatively weak. This seems a likely possibility since strong interocular interactions which are powerful enough to shift the LGN X/Y ratio are only observed in chronically paralyzed and not acutely paralyzed animals (Salinger et al., 1977b; Garraghty et al., 1982).

The enhancement of interocular interactions induced by monocular paralysis could be due to either the formation of new circuits in or outside the LGN which promote binocular interactions, or an alteration in neural activity in already existing circuits. Of these, the latter seems more likely, since the intensity of interocular interactions associated with chronic monocular paralysis can be modulated by anesthesia state (Garraghty et al., 1982; Schroeder et al., 1984).

A second possible reason for the failure to observe powerful interocular interactions under conventional recording conditions may have to do in part with the use of anesthesia and/or paralytic agents. Previous work on visually mediated interocular interactions (e.g., Sanderson et al., 1971; Singer, 1970; Rodieck & Dreher, 1979) has involved the use of anesthetized and systemically paralyzed preparations. The results of this experiment along with others (Schroeder et al, 1984; Garraghty et al, 1982) have shown that at least

the use of anesthesia severely attenuates the relative strength of interocular interactions in LGN associated with chronic monocular paralysis. For example, shifting from sedation to anesthesia in chronically monocularly paralyzed cats restores X/Y ratio immediately to normal values in laminae innervated by either the paralyzed or mobile eye. Thus, the use of anesthesia may alter neural processes in a way which masks the physiology of binocular interactions in LGN. In any case, using the unanesthetized, monocularly paralyzed preparation reveals that the LGN is capable of very strong visually mediated interocular interactions.

Neural substrate for visually mediated interocular interactions in LGN. Several investigators have proposed that intrinsic neurons or interneurons (Golgi type II) which occur in abundance in various forms within and between all LGN laminae serve as the neural substrate for lateral as well as translaminar inhibitory interactions. (Guillery, 1971; see Szentagothai, 1973). In the LGN the dendrites of interneurons form synapses with relay cells as well as with dendrites of other interneurons and represent as much as 20-25% of LGN total cell population (Geisert, 1980; Levay & Ferster, 1979; Weber & Kalil, 1983). More recently, these neurons have been shown to utilize an inhibitory transmitter substance, gamma-aminobutyric acid (GABA) (Fitzpatrick, Penny, Schmechel, & Diamond, 1982; Montero & Singer, 1984a), which when exogenously applied exerts a powerful inhibitory action on LGN relay cells (Curtis & Tebecis, 1972; Morgan, Sillito, Wolstencroft, 1974).

Other investigators have argued that inhibitory interactions need

not be confined to intrinsic circuits of the LGN (see Singer, 1977), but may also involve connections between LGN and adjacent thalamic nuclei such as those that exist between LGN and the perigeniculate nucleus (PGN) (Ahlsen et al., 1978; Ahlsen & Lindstrom, 1982; Friedlander et al., 1979, 1981). Comparisons between the latency of excitatory responses in the PGN and of inhibitory responses in the LGN after optic chiasm stimulation suggest that the PGN mediates recurrent inhibition of LGN relay cells (Dubin & Cleland, 1977; Lindstrom 1982). It has also been shown that virtually all neurons in PGN use the inhibitory agent GABA as a transmitter substance (Montero & Singer, 1984b). It seems reasonable to assume that the neural circuits which support these visually mediated interocular interactions, whether they be intrinsic or extrinsic to the LGN, are also involved in supporting nonvisual, proprioceptively mediated interocular interactions (see above). If so, then it appears that a great deal of sensory integration between the two eyes occurs at the first relay between eye and visual cortex.

The Integration of Retinal and Extraretinal Signals in LGN

It is no longer appropriate to think of the LGN as a simple relay between the retina and visual cortex, but rather as a possible site along the visual pathway where retinal and extraretinal signals converge. This suggestion has been put forth by several investigators who have demonstrated responses among visually driven cells in the LGN, associated with either saccadic eye movements (see Burke & Cole, 1978) or passive eye movements (Donaldson & Dixon, 1980). Several attempts have also been made to identify the possible sources of such extraretinal responses in the LGN in order to understand their role in

the processing of visual information. In general terms, extraretinal signalling along visual pathways can be traced to an efferent or an afferent source.

Efferent signals as a source of extraretinal input to the LGN. Many investigators have suggested that corollary discharges arising from neural signals generated in oculomotor centers of the brainstem and/or frontal cortex are the source of the extraretinal signals converging on LGN (e.g., Freund, 1973; Jeannerod et al., 1979; Holst, 1954; Sperry, 1950). In the literature, attempts have been made to interpret such interactions as the neuronal basis for perceptual adjustments needed to help keep the visual world stable during an eye movement (Holst, 1954; Jeannerod et al., 1979; Sperry, 1950). As a result, the concept of corollary discharge has been closely related to Helmholtz's outflow theory (1867/1962) in which he proposed that knowledge about eye position comes from the effort of will put forth in moving the eye. Support for outflow theory comes from a variety of experimental investigations which reveal that when the eye is passively displaced, the target rather than the eye is perceived as moving (Brindley & Merton, 1960; Helmholtz, 1867; Irvine & Ludvigh, 1936). Consistent with these observations, is the finding that when the eye is restrained or reversibly paralyzed prior to an attempted eye movement, the target is perceived as being displaced in the direction of the attempted but not executed movement (Brindley & Merton, 1960; Helmholtz, 1867; Matin et al., 1982; Stevens et al., 1976; West, 1932).

Other attempts have also been made to relate corollary discharges in the LGN to the elevation in visual threshold which occurs with a

saccade (Jeannerod, 1972; Latour, 1962; Volkmann, 1962; Zuber & Stark, 1966), since accompanying a saccade is a decreased responsiveness to visual stimulation among LGN relay cells (Adey & Noda, 1973; Cohen, Feldman, & Diamond, 1969; Noda & Adey, 1974; Noda 1975a). Additional evidence has shown however, that the movement of retinal images during a saccade and not the eye movement per se may be of considerable importance to the elevated visual threshold (Mackay, 1970; Noda & Adey, 1974). Further, the depression in LGN cell excitability which accompanies a saccade does not seem to be supported by central influences coordinated with efferent motor impulses, since such responses proved to be present only when saccades were made in the light and not in the dark (Noda, 1975b).

In conclusion, the concept of corollary discharge implies that outflow information from oculomotor centers can be utilized by central visual structures to regulate concomitant sensory messages. Presently, the psychophysical evidence relating outflow to visual function is not clearly supported by the available physiological evidence. Unfortunately, the present experiment cannot help to clarify this issue since only inflowing extraretinal signals were manipulated.

Afferent signals as a source of extraretinal input to LGN. Sherrington (1918) was the first to suggest that inflowing signals from proprioceptors located in extraocular muscles of the eye reach the brain and are utilized for visuomotor control. Since Sherrington, the idea has received both pyschophysical and neurophysiological support. Recently, an extraretinal signal of considerable magnitude arising from the orbit of the eye has been isolated. This signal can be be used to

help locate visual targets when retinal cues are unavailable (Skavenski, 1971; Skavenski, 1972; Skavenski & Steinman, 1970). Neurophysiological correlates for this perceptual ability have also been demonstrated. For example, in the cat when the eye is moved about its orbit in a passive fashion (thus excluding outflow) and in the dark, causing extraocular muscles to stretch, phasic unit activity has been recorded in the LGN (Donaldson & Dixon, 1980), visual cortex (Ashton et al., in press; Buisseret & Maffei, 1977) and lateral supersylvian areas (Donaldson, 1979). The source of inflowing extraretinal signals has been traced to proprioceptors in EOMs (see Batini, 1979) whose sensory afferents enter the brain along the ophthalmic branch of the trigeminal nerve (Alvarado-Mallart, Batini, Buisseret-Delmas, & Corvisier, 1975; Batini et al., 1975; Buissert-Delmas, 1976; Porter & Spencer, 1982). The present experiment also supports the idea that orbital proprioceptive signals reach visual pathways, since in the LGN, substantial shifts in the X/Y ratio were observed after afferent fibers from EOM proprioceptors were sectioned.

A proposed role for proprioception in binocular vision and binocular depth perception. On a conceptual level, there are good reasons to believe that sensory feedback from EOMs could play an important role in binocular vision and binocular depth perception (Carpenter, 1977). For example, proper synthesis of one image from two retinal images requires precise information about the position of each eye in its orbit. Simple geometric considerations reveal that for binocular depth perception absolute distance of an object to the eye is computed using both retinal and extraretinal cues, namely, retinal

disparity cues and ocular vergence information, respectively. If binocular vision and binocular depth perception rely on orbital proprioceptive signals, then visual structures like the LGN and visual cortex which are sensitive to input from the two eyes as well as eye position information, may serve as the neuronal basis for such capabilites.

Recently, a substantial amount of experimental evidence has accumulated which supports the idea that orbital proprioceptive signals are critical for certain aspects of binocular vision. For example, several investigators have found that the proportion of binocularly activated neurons in visual cortex of kittens is substantially lower than normal when proprioceptive afferents are interrupted by unilateral transection of V (Maffei, 1979; Berardi, Bisti, Fiorentini & Maffei, 1981; Trotter, Fregnac & Buisseret, 1981). Binocular depth perception is also impaired in kittens with normal visual experience by unilateral section of extraocular afferents (Graves, Trotter & Fregnac, 1984). In adult cats, bilateral section of extraocular afferents impairs the stability of eye position in the dark (Fiorentini & Maffei, 1977), and leads to abnormalities in visually guided jumping and visual depth discrimination (Fiorentini, Berardi & Maffei, 1982).

Although the above deficits seem to involve interactions between visual and proprioceptive signals in visual cortex, the LGN could represent the first relay in the visual pathway to visual cortex where retinal and extraretinal signals begin to interact. There are two possible routes by which orbital proprioceptive signals converge on visual cortical cells: a direct route which would involve afferents

from trigeminal nerve nuclei located in brainstem (Manni et al., 1971, 1972, 1974) ascending to visual cortex, or an indirect route which would involve afferents from brainstem to LGN, and then via geniculo-cortical afferents (Giesert, 1980; see Rodieck, 1979) to visual cortex. Whether the LGN provides the basis of such interactions in visual cortex is not yet known but it would seem likely since inputs from LGN cells provide the neural circuitry in visual cortex necessary for visually mediated, binocular interactions (see Gilbert, 1984; Rodieck 1979).

Orbital Proprioceptive Signals and Experience Dependent Changes along Visual Pathways

In a broader context, an additional role for orbital proprioception has emerged which is based on the idea that such signals are necessary for manifestations of visual plasticity.

Orbital proprioceptive signals and the establishment of visual plasticity. Many studies have indicated that early visual experience can modify the receptive field characteristics of visual cells (e.g. Barlow, 1975; Fregnac & Imbert; 1984; Movshon & Van Sluyters, 1981). Singer (1982) has hypothesized that proprioceptive signals from extraocular muscles may in part be necessary for manifestations of visual plasticity occurring early in development (see also Fregnac & Imbert, 1984). Singer maintained that the onset of an eye movement predicts with great reliability that new information will arrive within a few hundred milliseconds. Proprioceptive signals could thus serve as an "alerting signal" for visual cells to prepare for the arrival of new information.

There is mounting evidence that supports Singer's hypothesis,

indicating that visually mediated, experience dependent changes occurring in the developing visual system are controlled by orbital proprioceptive signals. For example, several studies have shown that during the critical period of development, the formation of normal cortical receptive field properties (e.g., orientation selectivity and binocularity) fails when proprioceptive cues from extraocular muscles are removed by bilateral trigeminal nerve section (Buisseret & Gary-Bobo 1979; Buisseret & Singer, 1983; Trotter, Fregnac, & Buisseret 1983; Trotter, Gary-Bobo, & Buisseret, 1981). A similar failure to produce experience-dependent changes in visual cortex is observed when all eye movement activity is suppressed by anesthesia and systemic paralysis (Freeman & Bonds, 1979; Buisseret, Gary-Bobo, & Imbert; 1978). Other investigators have also shown that disruptions in proprioceptive signalling produced by cyclotorsion of one eye (Singer, Tretter, & Yinon, 1982; Singer, Yinon, & Tretter, 1979) or unilateral section of V (Imbert & Fregnac 1983; Trotter et al., 1983) interferes with the usual shifts in cortical ocular dominance produced by brief periods of monocular occlusion. Finally, it also appears that orbital proprioceptive signals may be critical for the acquisition of certain sensorimotor capabilities. For example, dark-reared kittens which had one eye surgically paralyzed, or its proprioceptive afferents interrupted, fail to develop normal visual guidance when exposed to light (Hein, Vital-Durand, Salinger, & Diamond, 1979; Hein & Diamond, 1983).

Taken together these studies suggest that the degree of susceptibility to visual experience, either binocular or monocular, is

very much dependent upon whether proprioceptive signals reach visual pathways in normal fashion.

Singer (1982) has suggested that neurons in the medial nuclear complex of the thalamus which seem to be involved in stimulus selection (Orem, Schlag-Rey, & Schlag, 1973; Watson & Heilman, 1979) may provide the basis of a "gating" signal by which orbital proprioceptive signals converge upon ascending visual pathways. When large lesions are made in the dorsal medial aspect of the thalamus, it results in the failure to observe experience dependent changes in visual cortex (Singer, 1982). Singer & Rauschecker (1982) have made the complementary observation that central thalamic stimulation when linked with monocular visual stimulation facilitated the shift in ocular dominance toward the stimulated eye and the acquisition of mature receptive fields. In both of these studies the targeted area was the internal medullary lamina (IML) of the thalamus, an area whose fibers project to several thalamic nuclei, including the LGN (Scheibel & Scheibel, 1966) as well as visual cortex (Miller & Benevento, 1979). Neurons in the IML discharge soon after the eye assumes a new position (Schlag & Schlag-Rey, 1983). Thus, these cells may provide the basis of a neural signal necessary for manifestations of visual plasticity.

Neural plasticity, brain catecholamines, and orbital proprioceptive signals. In addition to the above manipulations, in one other circumstance, visual stimuli fail to modify cortical receptive fields during the critical period of development, namely, when cerebral catecholamines are depleted (Bear et al., 1983; Kasamatsu & Pettigrew, 1976; 1979; Kasamatsu, Pettigrew, & Ary, 1981; Paradiso, Bear, &

Daniels, 1983) These authors report that the depletion of cerebral catecholamines, accomplished by treating kittens intracranially with the pharmacological agent 6-hyroxydopamine, a neurotoxin specific for catecholamine containing nerve terminals (Jonsson, 1980), prevents the ocular dominance shift that normally accompanies brief periods of monocular occlusion. Moreover, when the catecholamine, norepinephrine is replaced by continuous intracranial microperfusion, the developing visual cortex will again become susceptible to visual experience (Kasamatsu, Pettigrew, Ary, 1979, 1981; Pettigrew & Kasamatsu, 1978). Treating monocularly paralyzed cats with 6-hyroxydopamine has also resulted in the failure to observe the experience dependent changes in the X/Y ratio recorded in the LGN of the adult cat (Guido et al., 1982). These failures to detect plasticity when cerebral catecholamines are depleted may be related to the functional disruption of ascending proprioceptive signal transmission.

There are good reasons to believe that brainstem catecholamine neurons may be involved in the transmission of orbital proprioceptive signals. For example, in the cat, virtually all noradrenergic containing cell bodies originate in the locus coeruleus complex, a diffuse system of nuclei located in the rostral pontine tegmentum (Chu & Bloom, 1974; Jones & Moore, 1974). The ascending fibers of the locus coreuleus complex give rise to an extremely widespread pattern of projections which terminate in several structures located throughout the brain (see Moore & Bloom, 1979), including LGN (Chu & Bloom, 1974; Maeda et al., 1973; Macbride & Sutin, 1976) and visual cortex (Ikatura, Kasamatsu, & Pettigrew, 1981; Tork & Turner, 1981). Moreover, orbital

proprioceptive pathways which originate in the brainstem overlap substantially with catecholamine containing nuclei and projections of the locus coeruleus complex (see Brodal, 1981). This anatomical link between catecholamine containing neurons and orbital proprioceptive signals is further strengthened by a number of electrophysiological studies which demonstrate that destruction of the ascending catecholamine projection system results in the termination of all eye movement related activity in LGN and visual cortex (Buguet, Petitjean, & Jouvet, 1970; Jouvet, 1972; Laguizzi, Petitjean, Pujol, & Jouvet, 1972; Kasamatsu & Pettigrew, 1978; Sakai, Petitjean, & Jouvet, 1976). Thus, it is likely that treating cats with a catecholamine depleting agent, in addition to destroying virtually all neurons which utilize catecholamines as a transmitter substance, also results in the functional disruption of ascending proprioceptive signal tranmission, and could thus explain the failure to detect experience dependent changes along visual pathways.

Orbital proprioception and maintenance of visual plasticity. In addition to its role in controlling manifestations of visual plasticity, proprioceptive signals may also be necessary to maintain experience dependent changes among visual pathways. In the present experiment, the removal of orbital proprioceptive signals from the mobile eye by unilateral section of V resulted in the complete and permanent restoration of encounter rates for LGN cells. Further support for the idea that proprioceptive signals are involved in the maintenance of visual plasticity, comes from pharmacological experiments performed on monocularly paralyzed cats in which the effects of monocular paralysis

were blocked, possibly by disrupting proprioceptive input to the LGN. For example, a similar failure to maintain the physiologic consequences of monocular paralysis occurs during electrophysiological recording sessions in which chronic cats are anesthetized (Garraghty et al., 1982; Schroeder et al., 1984). The reported sites of central action for anesthetic agents involve ascending pathways of brainstem (Darbinjar et al., 1971; French et al., 1953), which overlap substantially with fibers of passage originating in the trigeminal sensory nuclei (see Brodal, 1981), and which most likely route proprioceptive signals to central visual structures. Since during anesthesia activity along such pathways are completely silenced (Darbinjar et al., 1971; French et al., 1953) the induction of anesthesia could cause a temporary cessation of proprioceptive signal transmission.

The Relationship Between Strabismus and Monocular Paralysis

Strabismic amblyopia is a common clinical condition which involves a misalignment of the visual axes of the two eyes during binocular fixation. The two most common forms of strabismus are the convergent type (esotropia) in which one eye is deviated inwards with respect to the other, and the divergent type (exotropia) in which the visual axis of one eye is rotated outward. Strabismics possess poor stereoscopic vision, and often have a reduced acuity or amblyopia in the deviated eye (Duke-Elder & Wybar, 1973; Flax, 1983).

There are several potential causes of strabismus ranging from anatomic or mechanical interferences with eye movements because of congenital malformation or trauma, to functional or innervational abnormalities (see Flax, 1983). At first glance, the management of

strabismus would seem simple and straightforward. If the eyes are misaligned, isolate the responsible factor and select the appropriate means (surgery or orthoptics) to relieve it. Unfortunately, few aspects of eye care are as complex and difficult as the treatment of strabismus (see Flax 1983; Jampolsky, 1978). It is generally agreed among clinicians however, that successful management of strabismus is possible if treatment is initiated early in life, whereas adult strabismus, arising out of childhood or acquired later in life has a very poor prognosis for functional recovery (Duke-Elder & Wybar, 1973; Scott, 1983). This clinical observation is entirely consistent with one of the most central concepts to emerge in developmental neurobiology, namely, that early visual experience during a sensitive period of development has a dramatic effect on the establishment and maintenance of normal visual function (e.g., Movshon & Van Sluyters, 1981). As a result, efforts directed towards an understanding of the neural basis for the perceptual defects associated with strabismus have largely focused on the use of animal models in which strabismus has been induced early in life, orthoptically with prism goggles (e.g., Bennett, Smith, Harwerth, & Crawford, 1980; Crawford & Von Noorden, 1980; Van Sluyters & Levitt, 1980), or surgically by unilateral eye lid suture (e.g., Hubel & Wiesel 1970) or by section of one or more of the extraocular muscles (e.g., Hubel & Wiesel, 1965; Von Noorden & Dowling, 1970). Unfortunately for the clinician, the use of a developing organism as an animal model has been inadequate in mimicking certain aspects of the symptomatology of strabismus (Jampolsky, 1978; Marg, 1982). For a complete understanding of the pathology underlying the perceptual defects associated with

strabismus, further exploration of additional animal models would seem necessary, with the hope that, in the aggregate, they may provide a composite for the analysis and treatment of strabismus. Monocular paralysis may serve as one of these supplemental models, because of the similarities between it and strabismus.

Adult-onset monocular paralysis as an animal model for strabismus. Strong parallels exist between strabismus, the human clinical condition, and adult-onset monocular paralysis. For example, both result in a misaligned visual axis, with one eye deviated with respect to the other, which greatly diminishes the ability to achieve or sustain alignment. Strabismus involves amyblyopia in the deviated eye which seems to be confined to areas of central visual space (Hess, 1982; Hess, Campbell, & Zimmern, 1980; Sireteanu, 1982; Sireteanu & Fronius, 1981). Several investigators maintain that this amblyopic deficit is primarily an adaptive response on the part of the patient to suppress anomalous visual signals, which if left unchecked would give rise to diplopic vision (Flax, 1983; Jamplosky, 1978). Further, such a process seems to be centrally mediated and not retinal in origin (Hess, 1982; Hess, Campbell, & Greenhalgh, 1978; Sireteanu, 1982; Jampolsky, 1978). Finally, even after a prolonged period of strabismus, the suppression of visual inputs is partially reversible when measures are taken to relieve ocular misalignment (Scott, 1983).

Similarly, monocular paralysis is believed to trigger a centrally mediated, physiologic process sensitive to abnormal patterns of binocular stimulation which arise from ocular misalignment (Garraghty et al., 1982). Although acuity deficits have not been explored in

monocular paralysis, in this preparation an active physiologic mechanism suppresses visual inputs among X cells relative to Y cells, in the areas of the LGN confined to representations of central binocular visual space (Garraghty et al., 1982). This suppression of X cells relative to Y cells in areas of the LGN which represent central visual space could represent the neural basis for the circumscribed (central areas) acuity deficits in strabismus, since high spatial resolution is a perceptual capacity mediated by the X cell pathway (see Lennie, 1980). Further, the results from the present experiment indicated that the suppression of X cells is amenable to reversal when sensory modifications arising from ocular misalignment are eliminated. Finally, monocular paralysis, in addition to supressing visual inputs among X cells in the LGN, also results in a reduction in the proportion of binocularly driven neurons in visual cortex (Maffei & Fiorentini, 1976; Fiorentini et al., 1979). This decline in binocular excitatory convergence onto single cortical cells may account for the clinical observation that strabismics usually possess poor stereoscopic vision (Duke-Elder & Wybar, 1973).

The role of retinal signals in strabismus. Most clinicians maintain that ocular sensory-motor coordination lies at the heart of strabismic amblyopia (e.g., Jampolsky, 1978). Presently, the management of strabismus has focused primarily on relieving retinally mediated anomalies which arise from ocular misaalignment (e.g., see Scott 1983). Using monocular paralysis as a model to understand the neural correlates of strabismus has revealed that retinally mediated abnormalites (e.g., exaggerated patterns of retinal disparity) are critical in producing the suppression of X cells relative to Y cells in LGN (Salinger et al.,

1980). Further, the aspects of the present experiment which deal with the removal of retinal output from the mobile eye are also consistent with current treatment rationales: when abnormal patterns of retinal stimulation are eliminated there is a functional recovery of normal binocular vision. However, improper ocular alignment in strabismus produces two classes of stimulus distortions: retinal ones in the form of abnormal patterns of retinal disparity, and extraretinal ones in the form of oculomotor/proprioceptive asymmetries. Unfortunately, the nonretinal class has received very little experimental investigation, and is not the primary focus of attention when treating strabismus. The use of monocular paralysis as an animal model, however, has led to the suggestion that these signals figure prominently in strabismic amblyopia.

The role of orbital proprioceptive signals in strabismus. Recently, a good deal of evidence has surfaced which underscores the importance of extraretinal cues in strabismus. First, Steinbach & Smith (1981) have demonstrated that strabismic patients possess an altered ability to use proprioceptively derived cues to locate targets in a dark surround. Further, patients who have undergone repeated extraocular muscle surgery to correct the rotation in the deviated eye become worse rather than better at using such cues. This subsequent impairment is due most likely to the formation of scar tissue or the actual destruction of proprioceptors in the musculotendenious junction (Richmond, Johnston, Baker, & Steinbach, 1984). This latter finding may help explain why repeated surgeries despite proper ocular alignment generally have poor functional results (Flax, 1983; Scott, 1983).

In an attempt to dissociate the effects of retinal and nonretinally mediated stimulation associated with strabismus, Maffei & Bisti (1976) found that kittens deprived of binocular vision from the day that strabismus was introduced resulted in a decreased proportion of binocularly driven cortical cells. These results indicate that altered motility of the eyes per se, is sufficient to disrupt binocular interactions. Further, these results suggest that symmetry in the flow of information from EOMs to visual structures may contribute substantially to the neural deficits which account for strabismus amyblyopia.

Experiments which involve monocular paralysis have also underscored the importance of orbital proprioceptive factors. For example, monocularly paralyzed cats deprived of binocular patterned stimulation still suffer a partial shift of the X/Y ratio in the LGN (Salinger et al., 1980), and a reduction in the proportion of binocularly driven cortical cells (Maffei & Fiorentini, 1976; Fiorentini & Maffei, 1974). Further, if both eyes are immobilized, thereby reducing the degree of asymmetry between the two orbits, there is only a relatively minor effect on cortical binocularity (Maffei & Fiorentini, 1975) or on LGN physiology (Schroeder & Salinger, 1978). These results are complemented by the present study in which the effects of asymmetric ocular motility were relieved by sectioning orbital proprioceptive afferents from the mobile eye. Following the unilateral section of V, the X/Y ratio in the LGN was restored to normal values. Taken together, these results suggest that research on the treatment of strabismus should additionally focus on nonretinal factors, particularly the nature of proprioceptive

signals arising from deviated visual axes.

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APPENDIX A

Statistical Summary Tables

Table A-1

Analysis of Variance on the Relative Frequency of LGN Cells for Paralyzed Eye Layers

Source	df	MS	F
Condition (C)	4	.03333	.42
Error	15	.08000	
Cell Type (CT)	2	5000768.9733	99.49**
CT x C	8	490213.2733	9.75
Error	30	50262.1333	
Recording Time (T)	4	.03333	.47
T x C	16	.01458	.20
Error	60	.07167	
CT x T	8	296094.9358	8.08**
CT x T x C	32	99137.5171	2.71*
Error	120	36638.1708	

*$p < .0001$

**$p < .0000$

Table A-2

Analysis of Variance on the Relative Frequency of LGN Cells for Mobile Eye Layers

Source	df	MS	F
Condition (C)	4	0	.55
Error	15	0	
Cell Type (CT)	1	3695936.7200	15.77**
CT x C	4	1730879.1700	7.38**
Error	15	234393.0267	
Recording Time (T)	4	0	0
T x C	16	0	0
Error	60	0	
CT x T	4	524657.9200	5.38***
CT x T x C	16	222127.1200	2.28*
Error	60	97513.3600	

*$p < .002$

**$p < .0002$

***$p < .0001$

Table A-3

Simple Interaction of Condition (C) x Recording Time (T) for Each Cell Type (CT) for Layers Innervated by Paralyzed Eye

Source	df	MS	F
C x T at CT (X cells)	15	97329.2	3.97*
C x T at CT (Y cells)	15	58037.0	2.38*
C x T at CT (unclass. cells)	15	39085.3	1.05

MS Error (pooled) = 24425.471

df Error (pooled) = 120

Layers Innervated by Mobile Eye

Source	df	MS	F
C x T at CT (X cells)	15	111063.6	2.27*
C X T AT CT (Y Cells)	15	111063.6	2.27*

MS Error (pooled) = 48756.68

df Error (pooled) = 60

*$p < .01$

Table A-4

Simple Main Effect of Recording Time (T) for Condition (C) for Each Cell Type (CT) in Layers Innervated by the Paralyzed Eye

Source	df	MS	F
T at C (ACMD/II + V) CT (X cells)	4	18774.7	.76
T at C (CHMP/II + V) CT	4	285276.5	11.60*
T at C (CHMP/II) CT		154766.7	6.33*
T at C (CHMP/V mobile eye) CT	4	186338.7	7.62*
T at C (CHMP/V para eye) CT	4	31575.6	1.29
T at C (ACMP/II + V) CT (Y cells)	4	94642.3	3.87*
T at C (CHMP/II + V) CT	4	175814.58	7.19*
T at C (CHMP/II) CT	4	127777.4	5.23*
T at C (CHMP/V mobile eye) CT	4	156765.9	6.41*
T at C (CHMP/V paralyzed eye) CT	4	40977.9	1.67

MS Error (pooled) = 24425.471

df Error (pooled) = 240

*$p < .01$

Table A-5

Simple Main Effect of Recording Time (T) for Condition (C) for Each Cell Type (CT) in Layers Innervated by the Mobile Eye

Source	df	MS	F
T at C (ACMP/II + V) CT (X cells)	4	1000943.4	2.07
T at C (CHMP/II + V)	4	206880.6	4.24*
T at C (CHMP/II)	4	84854.0	1.74
T at C (CHMP/V)	4	302542.6	6.21*
T at C (CHMP/V)	4	11362.7	.23

MS Error (pooled) = 48756.68

df Error (pooled) = 120

*$p < .01$

APPENDIX B

Individual Data

Table B-1

Relative Frequencies of LGN Cells Recorded Under Sedated Conditions before and after the Removal of V from Mobile Eye of Four Monocularly Paralyzed Animals

Cat 552 rLGN							(Hours)					
	Pre-op		0-5		5-10		25-30		30-35		95-100	
Layer A	%	N	%	N	%	N	%	N	%	N	%	N
X			60.0	3	42.9	3	62.5	5	25.0	1	40.0	2
Y	100	4	20.1	1	57.1	4	37.5	3	75.0	3	60.0	3
Unclass.			20.0	1								
Layer A1												
X	20.0	1	40.0	2	50.0	3	62.5	5	66.7	4	60.0	3
Y	80.0	4	60.0	3	50.0	3	37.5	3	33.3	2	40.0	2

Cat 550 rLGN							(Hours)					
	Pre-op		0-5		5-10		20-25		25-30		30-35	
Layer A	%	N	%	N	%	N	%	N	%	N	%	N
X	20.0	1	75.0	6	85.7	6	40.0	2	44.4	4	28.6	2
Y	80.0	4	25.0	2	14.3	1	60.0	3	55.6	5	57.1	4
Unclass.											14.3	1
Layer A1												
X			50.0	1	61.7	2	80.0	4	50.0	2	71.4	5
Y	100	3	50.0	1	33.3	1	20.0	1	50.0	2	28.6	2

Cat 548 rLGN							(Hours)					
	Pre-op		0-5		5-10		20-25		40-45		45-50	
Layer A	%	N	%	N	%	N	%	N	%	N	%	N
X	23.5	4	40.0	2			66.7	4	66.7	2	75.0	3
Y	70.6	12	40.0	2			33.3	2			25.0	1
Unclass.	5.9	1	20.0	1					33.3	1		
Layer A1												
X	29.4	5	87.5	7			100	5	62.5	5	57.1	4
Y	70.6	12	12.5	1					37.5	3	42.9	3

Table B-1 (continued)

Cat 667 1LGN	(Hours)											
	Pre-op		0-5		5-10		20-25		25-30		30-35	
Layer A1	%	N	%	N	%	N	%	N	%	N	%	N
X	22.2	2	33.3	1	100	1	66.7	2	80.0	4	100	2
Y	55.6	5	66.7	2								
Unclass.	22.2	2					33.3	1	20.0	1		
Layer A												
X	25.0	1	100	7	100	3	100	11	80.0	8	75.0	3
Y	75.0	3							20.0	2	25.0	1

Table B-2

Relative Frequencies of LGN Cells Recorded Under Sedated Conditions before and after the Removal of V from the Paralyzed Eyes of Four Chronic Mononcularly Paralyzed Animals

Cat 668 rLGN							(Hours)					
	Pre-op		0-5		5-10		20-25		25-30		30-35	
Layer A	%	N	%	N	%	N	%	N	%	N	%	N
X	50.0	2										
Y	50.0	2			100	5	100	1	100	4		
Unclass.												
Layer Al												
X												
Y	100	4			100	3	100	3	100	2		

Cat 663 rLGN							(Hours)					
	Pre-op		0-5		5-10		20-25		25-30		30-35	
Layer A	%	N	%	N	%	N	%	N	%	N	%	N
X	16.7	1	21.4	3	25.0	2	20.0	1	14.3	1	25.0	2
Y	66.7	4	78.6	11	62.5	5	80.0	4	71.4	5	75.0	6
Unclass.	16.7	1			12.5	1			14.3	1		
Layer Al												
X	11.1	1	10.0	1	12.5	1			12.5	1	14.3	1
Y	88.9	8	90.0	9	87.5	7	100	4	87.5	7	85.7	6

Cat 559 rLGN							(Hours)					
	Pre-op		0-5		5-10		20-25		25-30		30-35	
Layer A	%	N	%	N	%	N	%	N	%	N	%	N
X	33.3	3	23.1	3	33.3	2			25.0	1		
Y	67.7	6	69.2	9	66.7	4	100	4	75.0	3		
Unclass.			7.7	1								
Layer Al												
X			16.7	1			50.0	1	16.7	2		
Y	100	2	83.3	5	100	4	50.0	1	83.3	10		

Cat 551 lLGN							(Hours)					
	Pre-op		0-5		5-10		20-25		25-30		30-35	
Layer Al	%	N	%	N	%	N	%	N	%	N	%	N
X	33.3	2			18.2	2	22.2	2	14.3	1		
Y	66.7	4			81.8	9	77.8	7	85.7	6		
Unclass.												
Layer A												
X												
Y	100	5										

Table B-3

Relative Frequencies of LGN Cells Recorded Under Sedated Conditions before and after the Removal of II + V from the Mobile Eye of Four Acute Monocularly Paralyzed Cats

Cat 543 rLGN					(Hours)					
	Pre-op		0-5		5-10		25-30		30-35	
Layer A	%	N	%	N	%	N	%	N	%	N
X	41.7	5	62.5	5	33.3	3	66.7	2	66.7	6
Y	50.0	6	25.0	2	22.2	2	33.3	1	33.3	3
Unclass.	8.3	1	12.5	1	44.4	4				
Layer A1										
X	60.0	9	66.7	4	80.0	4				
Y	40.0	6	33.3	2	20.0	1	100	1	100	6

Cat 547 rLGN					(Hours)					
	Pre-op		0-5		5-10		25-30		30-35	
Layer A	%	N	%	N	%	N	%	N	%	N
X	75.0	6	44.4	4	60.0	3	50.0	1	50.0	2
Y	25.0	2	33.3	3	20.0	1	50.0	1	50.0	2
Unclass.			22.2	2	20.0	1				
Layer A1										
X	66.7	4	71.4	5	28.6	2				
Y	33.3	2	28.6	2	71.4	5	100	2	100	2

Cat 545 rLGN					(Hours)					
	Pre-op		0-5		5-10		20-25		25-30	
Layer A	%	N	%	N	%	N	%	N	%	N
X	61.5	8	53.8	7			25.0	2		
Y	15.4	2	30.8	4			62.5	5	100	1
Unclass.	23.1	3	15.4	2			12.5	1		
Layer A1										
X	66.7	6	75.0	3			100	3	100	1
Y	33.3	3	25.0	1						

Cat 672 rLGN					(Hours)					
	Pre-op		0-5		5-10		20-25		25-30	
Layer A	%	N	%	N	%	N	%	N	%	N
X	50.0	2	46.7	7	66.7	2	25.0	1	50.0	3
Y	50.0	2	46.7	7					50.0	3
Unclass.			6.7	1	33.3	1	75.0	3		
Layer A1										
X	33.3	2	40.0	2	20.0				33.3	2
Y	66.7	4	60.0	3	80.0		100	4	66.7	4

Table B-4

Relative Frequencies of LGN Cells Recorded Under Sedated Conditions before and after the Removal of II from the Mobile Eye of Four Chronic Monocularly Paralyzed Animals

Cat 684 rLGN														
	Pre-op		(Hours) 0-5		5-10		20-25		25-30		30-35		45-50	
Layer A	%	N	%	N	%	N	%	N	%	N	%	N	%	N
X	25.0	2			83.3	5	50.0	2	25.0	3	14.3	1		
Y	75.0	6			16.7	1	50.0	2	75.0	9	85.7	6		
Unclass.														
Layer Al														
X														
Y	100	3			100	2			100	3	100	1		

Cat 541 rLGN														
	Pre-op		(Hours) 0-5		5-10		20-25		25-30		30-35		45-50	
Layer A	%	N	%	N	%	N	%	N	%	N	%	N	%	N
X	30.8	4	75.0	3	100	5	50.0	2	66.7	4	10.0	1	40.0	2
Y	46.2	6	25.0	1			50.0	2	16.7	1	80.0	8	60.0	3
Unclass.	23.1	3							16.7	1	10.0	1		
Layer Al														
X	9.1	1												
Y	90.9	10	100	1	100	1			100	2	100	1		

Cat 662 rLGN														
	Pre-op		(Hours) 0-5		5-10		20-25		25-30		30-35		45-50	
Layer A	%	N	%	N	%	N	%	N	%	N	%	N	%	N
X	25.0	1	100	2	60.0	6	66.6	2	37.5	3	40.0	2	33.3	1
Y	75.0	3			40.0	4	33.3	1	50.0	4	40.0	2	66.7	2
Unclass.									12.5	1	20.0	1		
Layer Al														
X	10.0	1	33.3	1	75.0	3			33.3	2			50.0	1
Y	90.0	9	66.7	2	25.0	1			66.7	4			50.0	1

Cat 679 lLGN														
	Pre-op		(Hours) 0-5		5-10		20-25		25-30		30-35		45-50	
Layer Al	%	N	%	N	%	N	%	N	%	N	%	N	%	N
X	25.0	1	50.0	7	50.0	2	33.3	1	40.0	4	23.5	4		
Y	75.0	3	42.9	6	50.0	2	66.7	2	60.0	6	76.5	13		
Unclass.			7.1	1										
Layer A														
X	22.2	2	100	2										
Y	77.8	7												

Table B-5

Relative Frequencies of LGN Cells Recorded Under Sedated Conditions before and after the Removed of II + V from the Mobile Eye of Four Chronic Monocularly Paralyzed Animals

Cat 683 1LGN							(Hours)					
	Pre-op		0-5		5-10		20-25		25-30		30-35	
Layer A1	%	N	%	N	%	N	%	N	%	N	%	N
X					33.3	3	20.0	1	17.6	3		
Y	66.7	2			50.0	3	80.0	4	70.6	12		
Unclass.	33.3	1			16.7	1			11.8	2		
Layer A												
X	22.2	2			33.3	1	100	1	25.0	1		
Y	77.8	7			66.7	2			75.0	3		

Cat 549 rLGN							(Hours)					
	Pre-op		0-5		5-10		20-25		25-30		30-35	
Layer A	%	N	%	N	%	N	%	N	%	N	%	N
X	22.2	4	37.5	3	80.0	4			20.0	2		
Y	66.7	12	62.5	5	20.0	1	75.0	3	70.0	7	100	3
Unclass.	11.1	2										
Layer A1												
X	20.0	2	100	2	66.7	2	100	1				
Y	80.0	8			33.3	1			100	3	100	1

Cat 535 rLGN							(Hours)					
	Pre-op		0-5		5-10		20-25		25-30		30-35	
Layer A	%	N	%	N	%	N	%	N	%	N	%	N
X			83.3	5	100	7	75.0	3	11.1	1	25.0	1
Y	60.0	3	16.7	1			25.0	1	88.9	8	75.0	3
Unclass.	40.0	2										
Layer A1												
X	25.0	1	66.7	2			33.3	1	50.0	1		
Y	75.0	3	33.3	1	100	7	66.7	2	50.0	1		

Cat 546 rLGN							(Hours)					
	Pre-op		0-5		5-10		20-25		25-30		30-35	
Layer A	%	N	%	N	%	N	%	N	%	N	%	N
X			42.9	3	83.3	5			20.0	1	16.7	2
Y			42.9	3			40.0	2			83.3	10
Unclass.			14.3	1	16.7	1			40.0	2		
Layer A1												
X			12.5	1	55.6	5			25.0	1		
Y	100	6	87.5	7	44.4	4			75.0	3	100	2