PLASTICITY IN THE CAT VISUAL SYSTEM

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Abstract

Behavioral and electrophysiological techniques have been used to study plasticity in the cat visual system both during and after the critical period for development of cortical binocularity. Both kittens reared with unilateral or bilateral eye rotation and adult cats given monocular rotations after the critical period showed good visuomotor adaptation to the rearranged visual information. All animals were able to learn a brightness discrimination. However, the three animals with monocular rotations of more than 120° were unable to learn oriented pattern discriminations although kittens raised with combined bilateral rotations of approximately 160° were able to learn even the most difficult orientation-discrimination. Apart from this there did not appear to be any significant correlation between rate of learning and angle of rotation.

All animals who learned the pattern discriminations showed considerable, though incomplete interocular transfer as assessed by improvement in initial performance and by savings and errors to criterion with the second eye as compared with the first.

Electrophysiological examination of area 17, in the kittens raised with monocular or binocular rotations, indicated the involvement of factors other than disparate visual input to the two retinas and asymmetrical eye movements per se in the breakdown of cortical binocularity seen in strabismic animals. Although most of the neuronal properties of area 17 were comparable to those reported previously for animals with unilateral rotations, some evidence for physiological adaptation to monocular and binocular rotation was seen in the corticotectal cells of layer V. A large proportion of the binocular corticotectal cells seen in animals with a total rotation angle of approximately 90° in both experimental groups showed significant shifts in direction selectivity such that the optimal stimulus direction was very similar in both eyes.

Plasticity of the visual cortex after the critical period was also examined electrophysiologically and it was found that the cortical effects of early monocular deprivation could be reversed when both the visual input to the brain and the extraocular afferents of the experienced eye were removed. After the combined treatments of pressure blinding and retrobulbar block of the normal eye approximately 50% of the units encountered could be shown to be influenced by the formerly deprived eye.

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General Introduction

The extent to which the nervous systems of vertebrates show plasticity and are subject to rearrangement as a function of experience has long been debated (see reviews, Hebb, 1949; Lippe, 1976; Sperry, 1945, 1971). Since the mid-1940's the weight of evidence has indicated that the basic neural substrate for behavior is genetically determined and prewired for function (Hunt and Jacobsen, 1974; Jacobsen, 1970; Sperry, 1943, 1944, 1945, 1961, 1971). More recently the emphasis of discussions of plasticity in mammals has shifted to center on the degree to which the innate pattern of neuronal connections can be modified by selective environmental influences. This thesis addresses three aspects of plasticity in the visual system of the cat. The first is behavioral plasticity following displacement of the visual information to the two retinae by surgical rotation of the eyeball. The second is a consideration of the synaptic changes or readjustments of the cortical neuronal properties which follow this environmental change during the development of the visual system. The third is an examination of the factors which under extreme conditions will elicit functional plasticity in the visual cortex of adult cat.

Many examples of behavioral plasticity following rearrangement of the sensory information to the mammalian brain have appeared over the last century. The first reports of humans wearing prisms which displaced the visual field, described a state of 'adaptation' or adjustment which followed prolonged wearing (Stratton, 1896, 1897). Stratton claimed that after several days of viewing the world through a monocular inverting prism his visuomotor responses adjusted to the point where they provided automatic compensation for the rearranged visual information. Since then behavioral adaptation to disparate visual images on both retinae produced by prisms has been reported in several adult mammalian species--in cats (Bishop, 1959), in normal monkeys (Foley, 1940; Hamilton, 1964), and in split-brain monkeys (Bossom and Hamilton, 1963; Hamilton, 1964, 1967). However, it appears that lower vertebrates such as amphibians (Sperry, 1943) and fish (Sperry, 1948) are not able to adjust their motor responses to compensate for either inversion or reversion of their sensory world, suggesting that although these animals are capable of extensive neural regeneration following lesions, etc., the pattern of reconnection is so rigidly wired that not even long term experience of a mismatch between the sensory input and motor output can elicit functionally more efficient behavior (Sperry, 1943). This has led people to wonder at what level of the nervous system behavioral plasticity occurs, and what is the particular neurophysiological basis for the adaptation seen in mammals.

Adaptation to a rearranged visual world is a particularly interesting form of neural plasticity since examples of such behavioral adjustments can be found in both juvenile and adult animals (Harris, 1965), suggesting that there are probably at least two different mechanisms, which are not necessarily related. In young animals the changes seen after eye rotation are possibly more closely related to normal visual development than to the 'adaptation' described by Stratton (1897) which occurs in an adult.

Over the last two decades much work has been done to examine the effects on primary visual cortex of various types of selective rearing (Barlow, 1975; Grobstein and Chow, 1976). In 1963, Wiesel and Hubel first described the effects on the cortex of depriving kittens of vision through one eye. Since then numerous papers have appeared elaborating the cortical effects of unilateral and bilateral deprivation (Wiesel and Hubel, 1965a) and the extent of recovery both during (Blakemore and Van Sluyters, 1974; Blasdel and Pettigrew, 1978; Movshon, 1976) and after the juvenile period (Wiesel and Hubel, 1965b). By way of such recovery experiments (Hubel and Wiesel, 1970) and reversing procedures, where the animal is forced to use the formerly deprived eye (Blakemore and Van Sluyters, 1974), a critical period or time when the cortex is sensitive to changes in binocularity has been defined. After this period only traumatic experiences such as removal of the experienced eye have been able to elicit reversal of the cortical effects of monocular deprivation during the first 12-14 weeks of a cat's life (Kratz, Spear and Smith, 1976).

Other environmental manipulations such as rearing with an artificially induced strabismus or with alternating monocular occlusion (Hubel and Wiesel, 1965) and stripe rearing (Hirsch and Spinelli, 1971) all indicate that disparate visual input to the two retinas alters the physiological properties of neurons in the striate cortex. Thus rearing animals with rotations of the visual field will result in the developing visual system receiving discordant information through the two eyes and can be expected to affect visual cortex.

The work presented here in Chapters I and II is an attempt at a systematic analysis of the degree and types of visuomotor and perceptual adaptation which follow surgical rotation of one or two eyes in visually inexperienced kittens and in adult cats. Chapter III is an electrophysiological examination of primary visual cortex as a possible locus of plasticity or adaptation to rotation of the visual field in young animals. Chapter III also compares the relative effects of unilateral and bilateral eye rotation at the time of eye opening on the development of cortical physiology. Chapter IV is a separate study examining the role of extraocular afferents in reversing the cortical effects of monocular deprivation after the critical period for development of binocularity (Blakemore and Van Sluyters, 1974; Hubel and Wiesel, 1970) is thought to be over.

These experiments have been pursued with behavioral and electrophysiological techniques in collaboration with Dr. Carol K. Peck of Pomona College, David P. Crewther of the Physics Division, Caltech, and Dr. John D. Pettigrew of the Biology Division, Caltech. Each chapter is presented as an independent entity with its own introduction and discussion of the relevant literature.

CHAPTER I

Perceptual Effects of Surgical Rotation of the Eye in Kittens[1]

Modifications of early visual experience--including stripe rearing, monocular deprivation, and artificial strabismus--affect both the response properties of neurons within the cat's visual cortex (Blakemore and Cooper, 1970; Hirsch and Spinelli, 1970, 1971; Hubel and Wiesel, 1965, 1970) and the perceptual capacities of the animal (Dews and Wiesel, 1970; Ganz, Hirsch and Tieman, 1972; Hirsch, 1972; Muir and Mitchell, 1975; Riesen, Kurke and Mellinger, 1953; Sherman, 1971). Since plastic changes also occur in the monkey's visual cortex (Baker, Grigg and von Noorden, 1974), such experiences are thought to be involved in the genesis of some deficiencies of visual perception in man (Mitchell, Freeman, Millodot and Haegerstrom, 1973; Mitchell and Ware, 1974; Movshon, Chambers and Blakemore, 1972). In addition, more subtle alterations of human visual perception may be linked to corresponding changes in cortical physiology: as with certain perceptual aftereffects which are commonly attributed to selective fatigue of cortical neurons (Coltheart, 1971).

Other perceptual rearrangements, such as those involved in adaptation to prismatic distortions, may not be so simply tied to alterations in the responsiveness of cortical neurons. In man and other higher mammals, rotation, inversion, or displacement of the retinal image leads to an initial perturbation of vision and visually-guided behavior, followed by partial adjustment to the altered input (Held and Hein, 1958; Kohler, 1955; Smith and Smith, 1962; Stratton, 1897). However,

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[1] This work has been published as Carol K. Peck and Sheila Gillard Crewther (1975), Brain Research 99, 213-219. Copyright held by Elsevier Scientific Publishing Co., Amsterdam.

the physiological bases of such readjustments remain largely unknown; in fact, Blakemore, Van Sluyters, Peck and Hein (1975) have recently reported that neurons of the cat's primary visual pathways, at least at the level of striate cortex, do not reorganize their physiological properties following rotation of one eye in infancy, although animals showed some visuomotor compensation to the rotation. The degree to which the kittens were able to use their rotated eyes was inversely correlated with the degree of rotation. The kitten with the least degree of eye rotation (30^o) showed visually guided reaching, whereas the other 3 whose eyes were rotated between 70^o and 115^o showed only simple visual behaviors, such as visual following and placing to a broad uninterrupted surface. They did not show more finely guided behavior.

Many questions remain about the visual capacities of kittens with rotated eyes, because only a small group was tested on relatively few problems. In particular, it is not clear if the rotated eye can discriminate visual forms, nor if the two eyes will show interocular transfer of perceptual discriminations.

In this paper, we report the results of discrimination training of 2 kittens with rotated eyes, plus further data on visually guided behavior in another group of 6 kittens with the same surgery. Since we wanted to study animals which would make maximal use of the rotated eye, we kept the rotations to less than 70^o and performed the operations at or before the time of natural eye opening. Three kittens had their normal eye closed by lid suture at 5 weeks of age in order to determine if 'forced use' of the rotated eye would facilitate the readjustment of visually guided behavior.

When the kittens were 2 months old, their vibrissae were cut and they were examined for simple visuomotor behavior; in the case of animals reared with both eyes open, black contact occluders were used to test the rotated and normal eyes separately. As can be seen in Table I, all of the kittens showed a high degree of visuomotor capacity when using the rotated eye. They showed visual following of both slowly and rapidly moving objects and visual placing (triggered extension) when slowly lowered to a broad, uninterrupted surface. In addition, they showed visually guided reaching of two types: (1) they hit accurately and precisely at balls and other small objects which were dangled at various locations within the visual field; and (2) when placed on a platform in front of an interrupted (pronged) surface of the type introduced by Hein and Held (1967), they reached directly and accurately for the prong, and avoided the gap between prongs, on at least 9 of 10 trials. Moreover, they performed well while running a simple obstacle course, and jumped accurately from table tops, grading the force of the jump to the distance between floor and table.

The visual behavior of these animals most closely resembles that of the kitten with the smallest rotation (30^{o}) from the previously published series. In fact, they surpassed that animal on the test of guided locomotion. All of these animals performed better than the previously reported animals with larger (70-115^{o}) rotations. Some of the present animals had rotations which approached 70^{o}; perhaps their greater visual skills are attributable to rotation at an earlier age than in the previously reported series (in which only 1 of 3 kittens with larger rotations was operated before 20 days of age).

Two of the kittens (DCN and ART) were trained on a series of two-choice visual discriminations, using food reward, in an apparatus similar to that of Myers (1962). Training began when the animals were 3-4 months of age and was monocular except for the first problem, which was trained binocularly. Black contact

TABLE I

Conditions of Rearing and Visual Behavior Using the Rotated Eye Alone

						Guided reaching		Guided locomotion	
Cats	Angle of rotation*	Reared with normal eye	Age at testing	Visual following	'Triggered' visual placing	To foil ball	To prong board**	Obstacle course	Jumping from height
AGR	-10°	closed	8 wks	yes	yes	yes	10/1	good	good
DCN	+10°	open	1 year	yes	yes	yes	10/0	good	good
ADL	+25°	closed	8 wks	yes	yes	yes	10/0	good	good
ATL	+30°	open	8 wks	yes	yes	yes	9/1	good	good
AAG	+40°	open	8 wks	yes	yes	yes	10/1	hesitant	hesitant
ART	+45°	open	1 year	yes	yes	yes	9/1	hesitant	hesitant
AGS	+55°	closed	8 wks	yes	yes	yes	10/0	good	good
ARS	+65°	open	8 wks	yes	yes	yes	10/0	good	good

* Positive numbers indicate intorsion of eye.

** Score is hits/misses.

lenses occluded vision through the unused eye. Each animal was trained for about 40 trials/day, 5-7 days/week. After criterion performance (90% correct on 2 consecutive days) was reached with each eye, 20 additional trials were run with both eyes occluded to test for leakage of light. Neither animal performed above chance under this condition on any problem, including the brightness problem.

The rotated eye can indeed discriminate visual forms, as both animals were able to learn all problems with each eye. Table II shows the trials which each cat required to reach criterion using each eye on the various discriminations. In some cases, the rotated eye was trained first (RE, for these animals); in other instances, the normal eye (LE) learned the problem first. As can be seen in Fig. 1, where each data point represents about 40 trials, the kittens took longer to learn and performed more erratically when only the rotated eye was open. Both eyes seem to learn at rates within the range of variation found in normally reared cats, although as mentioned above learning through the rotated eye was slower than through the normal eye. For example, when 7 adult cats were taught the square/plus problem by the same procedures, they required from 387 to 1132 trials to reach criterion. The mean number of trials to criterion was 664. DCN required 364 trials to learn the problem binocularly; yet when tested monocularly with the rotated eye, he performed no better than chance and required 768 additional trials to reach criterion. The number of trials which the rotated eye required to learn, though large, was still within the range of normally reared cats. ART also required a large number of trials to learn with his rotated eye, but did not exceed the number of trials of some normal cats.

As seen in Table II, a measure of savings in the number of trials which the second eye required to reach criterion was derived from the learning curves

TABLE II

Trials to Criterion, Per Cent Savings, and Change in Initial Performance on Four Discrimination Problems

	1. Square/plus			2. Dark/light			3. Vertical/horizontal			4. 45°/135°		
	Trials	Savings*	ΔI‡	Trials	Savings	ΔI	Trials	Savings	ΔI	Trials	Savings	ΔI
DCN	364 (both)	-36%	+20%	200 (RE)	+43%	+35%	507 (RE)	+100%	+50%	120 (LE)	-54%	+23%
	768 (RE)			80 (LE)			0 (LE)			401 (RE)		
ART	447 (both)	-28%	-16%	293 (RE)	+82%	+43%	274 (LE)	+36%	+61%	808 (RE)	+82%	+25%
	797 (RE)			29 (LE)			130 (RE)			80 (LE)		

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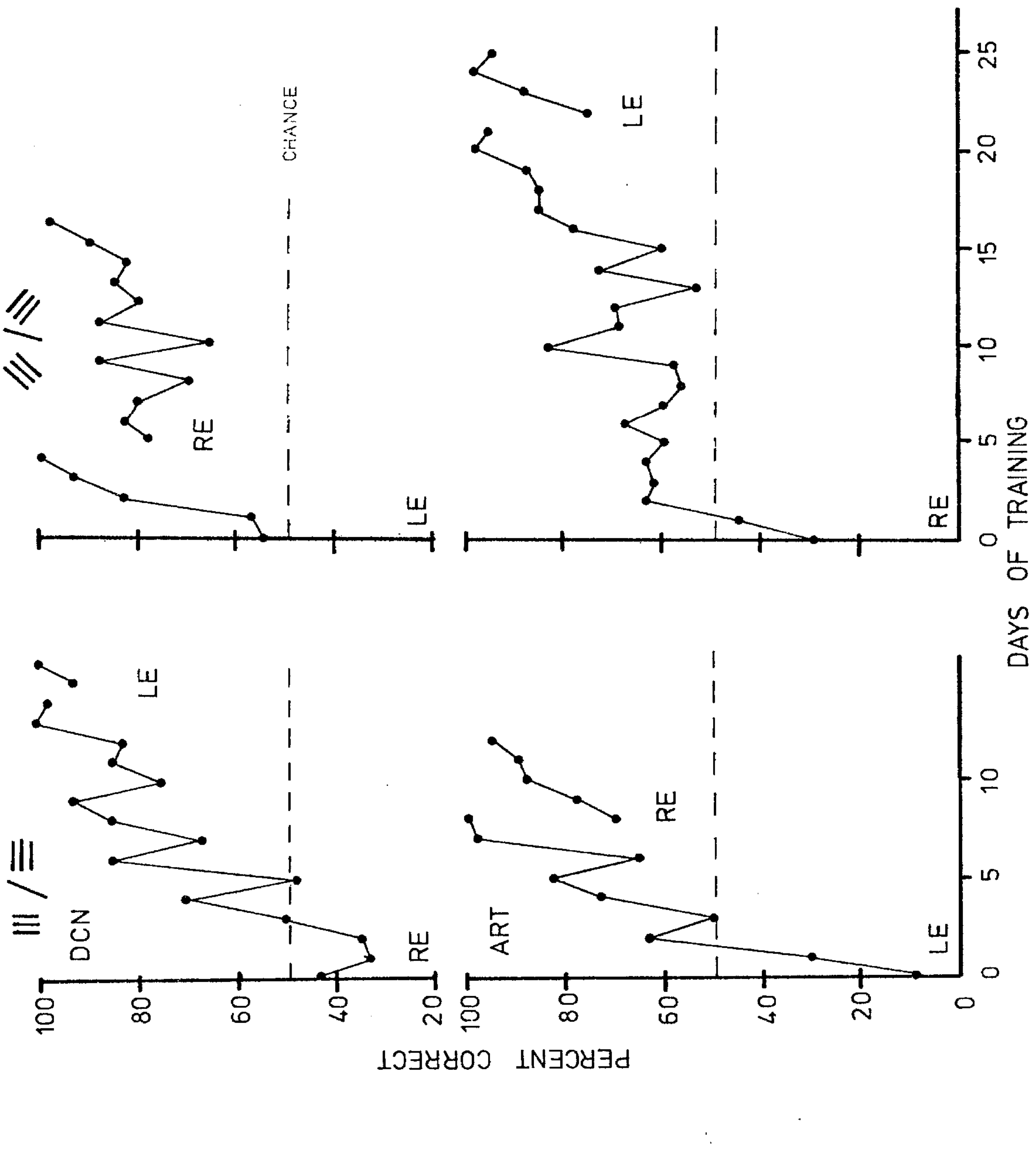
*Savings = $a - b/a + b \times 100$; where a is the number of trials to criterion in the first eye trained on a problem; b, in the second eye.

‡ΔI represents the differences between per cent correct responses on the first 40 trials with the two eyes.

Fig. 1. Learning curves for 2 cats (DCN, top row; ART, bottom row) on two problems (vertical/horizontal, on the left; diagonally oriented lines on the right). Each day of training represents approximately 40 trials. RE (right eye) was rotated; LE (left eye) was normally oriented. All training was monocular.


PERCENT CORRECT
DAYS OF TRAINING
CHANCE
DCN
ART
RE
LE
RE
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100
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40
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0
5
10
15
20
25

for each eye on each problem. If the animals had been reared normally, we could then use the savings scores as a simple measure of interocular transfer. However, when one eye but not the other has altered visual input, savings scores are an imperfect measure of interocular transfer, since the deprived eye will probably learn more slowly and more erratically than the normal eye. One way to assess interocular transfer in such a situation is to compare the learning rates of a large group of kittens, some of which initially learn a problem with the rotated eye and others of which learn the same problem with the normal eye first (Ganz, Hirsch and Tieman, 1972; Riesen, Kurke and Mellinger, 1953). Another, perhaps more powerful, way to assess interocular transfer is to compare the initial performance levels in learning each problem with the first and second eyes: if the animal performs substantially above chance on the first few trials using the second eye, then interocular transfer has surely occurred.

The data show a substantial amount of interocular transfer, even when based on savings in trials to criterion, except for the initial problem (square vs. plus). The amount of interocular transfer is indeed more impressive when the change in initial performance levels (per cent correct in the first 40 trials) is considered. Again, except for the first problem, the second eye performed well above chance. We have no immediate explanation for this apparent variability in interocular transfer on the first problem and on succeeding problems.

Though interocular transfer of the brightness and oriented-line problems was good, it was not perfect: in only one case did we find 100% savings. Furthermore, as expected, transfer from the rotated eye to the normal eye was better than transfer from the normal to the rotated. In one case DCN showed negative savings on the diagonally oriented line problem, which was first learned with the normal eye. However, even in this case, the learning curve for the rotated eye began well above chance (78% correct on the first 40 trials), and we therefore concluded that some interocular transfer had occurred and attribute the negative savings score to a generalized performance problem with the rotated eye. For these animals, savings scores based on errors are higher than those based on trials and thus lend support to this interpretation: 71%, 100%, and -33% for DCN on the dark/light, vertical/horizontal, and diagonal line problems, respectively; and 92%, 64% and 90% for ART on the same problems.

When the angle is small, eye rotation can be considered to be a special case of strabismus and to have a similar effect on interocular transfer. There are several reports that humans with a history of strabismus show much less interocular transfer of perceptual aftereffects than do normals (Mitchell and Ware, 1974; Movshon, Chambers and Blakemore, 1972). However, this reduction in interocular transfer seems to be greater than we find in our kittens and also greater than Sherman (1971) has found in artificially strabismic cats on discriminative learning problems. In order to resolve this point, larger numbers of subjects will be needed on tasks that are more nearly comparable.

Since cats with artificially induced strabismus have few binocular neurons within the visual cortex (Hubel and Wiesel, 1965), both Movshon _et al_. (1972) and Mitchell and Ware (1974) have inferred that the lack of interocular transfer in strabismic humans results from a virtual absence of binocular neurons. Thus, we might suggest, on the basis of the work of Blakemore _et al_. (1975), that our kittens showed better interocular transfer because they had a larger population of binocular neurons (about one-third of the sample, or 47 of 142 neurons). However, this argument loses plausibility in light of behavioral studies on monocularly deprived cats, which show some interocular transfer (Ganz, Hirsch and Tieman, 1972), but even fewer or no normally driven binocular neurons at the level of visual cortex (Hubel and Wiesel, 1970). Thus, it must be assumed that interocular transfer is not critically dependent on the presence of numerous, normally driven binocular neurons at this level of integration.

It is not clear whether substantial amounts of perceptual readjustment and interocular transfer should be expected in animals with larger rotations. Human subjects apparently show less complete adaptation to image rotations of about 90° than to smaller rotations or even to complete inversion (Smith and Smith, 1962). In our preliminary work, kittens with rotations of about 90° have shown only crude visuomotor skills; we are currently engaged in studies of their discriminative capacities in an attempt to determine what stimuli appear equivalent to both eyes.

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CHAPTER II

Pattern Discrimination and Visuomotor Behavior Following Rotation of One or Both Eyes in Kittens and in Adult Cats

Introduction

Examination of the behavior of animals with surgical rotation of one or two eyes around the optic axes provides a means of examining plasticity in the visuomotor system and of comparing the ability of the animal to relate two images of visual stimuli which have different orientations on the retina of the two eyes. The equivalence of the perceptions through the two eyes can be assessed from the degree of interocular transfer measured from normal eye to rotated eye and vice versa.

A considerable literature has accumulated over the last century on the subject of plasticity of visuospatial behavior in vertebrates following distortion of the visual world. In phylogenetic terms it appears that the visuomotor behavior of mammals, including humans (reviewed recently by Harris, 1965; Howard and Templeton, 1966; and Welch, 1974), is more adaptable to rearranged visual input than that of birds (Hess, 1956; Rossi, 1968), while amphibians (Sperry, 1943; Stone, 1944) and fish (Sperry, 1948) show essentially no visuospatial adjustment.

To date there are only two published studies examining how well mammals, in both cases, cats, are able to use rearranged visual information to learn oriented pattern discriminations through a rotated eye (Peck and Crewther, 1975; Mitchell, Giffen, Muir, Blakemore and Van Sluyters, 1976). These two reports have also briefly examined the ability of animals to demonstrate some interocular transfer of oriented pattern discrimination between two eyes receiving widely disparate visual input. However, little systematic work has been done to determine how equivalent the stimuli appear when viewed through displacing prisms or rotationally misaligned eyes. Rotation of the visual field can be produced either by the use of prisms or by surgical rotation of the eyeball.

Four reports on the visuomotor consequences of rotationally disparate experience in young kittens and adult cats have appeared recently. Blakemore, Van Sluyters, Peck and Hein (1975) initially reported partial adaptation of visuospatial coordination in four kittens and one adult cat with surgical rotation. Our preliminary findings (Peck and Crewther, 1975), and those of Mitchell et al. (1976) suggested even more accurate "visually guided" reaching and guided locomotion in animals with rotations up to 110°. Shinkman and Bruce (1977) also reported generally good visual behavior in kittens raised with small ±8° prismatic rotations of the visual field in both eyes. In contrast, Yinon (1975, 1976, 1977) has consistently reported that following eye rotation, most of his kittens--and particularly his adult cats--experienced serious and persistent behavior impairments.

In this paper we consider the perceptual capacities of a large sample of kittens with a wider range of angles of rotation on a more extensive series of two choice visual discriminations than elaborated in our earlier communication (Peck and Crewther, 1975). The visual skills of adult cats in which the rotation was performed after the critical period have also been examined as comparisons since there are many indications that early visual experience affects both the development of visual behavior and the neurophysiological properties of cells in the visual system (Barlow, 1975; Grobstein and Chow, 1975). Thus it seems reasonable that any adaptation which may follow distortion of the visual world would be maximized in animals raised without any previous experience of the normal visual world. In addition, we have studied a group of animals with both eyes rotated at the time of normal eye opening because it seemed that behavioral adaptation might be easier to observe in animals with both eyes rotated. After binocular rotation, it is less likely that either eye would be suppressed, as is sometimes reported for humans with strabismus. Alternatively, if there is no adaptation to early surgical rotation of the eye, behavioral deficits should be most obvious when both eyes are rotated. Most importantly, binocular rotations allowed us to create larger angles of disparity between the visual inputs of the two eyes without placing undue stress on the optic nerve of one eye. In general, our results confirm the previous reports of Blakemore et al. (1975), Peck and Crewther (1975), and Mitchell et al. (1976) for visuomotor adaptation and extend our own preliminary findings and those of Mitchell et al. (1976) about the ability of cats reared with large angles of rotation between the visual axes to learn oriented pattern discriminations and to transfer the information interocularly.

Methods

Twelve male and eight female kittens bred within our closed laboratory colony were used in this experiment. Two of the animals were given normal visual experience (group N), and two were given unilateral rotations at 6 months of age (group A, adult rotates). The other 16 kittens (group K, kitten rotates) had one (N = 13) or both (N = 3) eyes rotated at the time of natural eye opening. All kittens lived with their mothers and littermates in large pens where they could run freely until four months, at which time they were transferred to individual cages for housing in the main colony. The animal rooms were illuminated for 12 hr each day.

Surgery

All experimental animals were given a preoperative injection of either Ketamine hydrochloride (20 mg/Kg) or Equithesin (0.2 cc), and after sedation, were anesthetized with fluothane. The conjunctiva was then excised from around the eyeball and all of the extraocular muscles severed. Free rotation of the globe to at least 180° became possible after section of the muscles. The eye was rotated to approximately the desired angle (as judged by the angle of the fissured pupil and the position of the superior ophthalmic vein) and held gently in place with forceps for about 5 min. Very little rerotation to the normal orientation seemed to occur after this procedure. A drop or two of a broad-spectrum ophthalmic antibiotic ointment was routinely applied. The duration of the surgery was approximately 20 min; the kittens were usually active again within 30 min after which they were returned to their mothers and littermates.

Healing proceeded without complications; very rarely did a kitten develop any sign of corneal clouding or infection; the few that did are not included in the data reported. No attempt was made to prevent the muscles from reattaching, and eye movements were first observed about 6-8 days after surgery in young kittens. Older animals began to make small eye movements within 4 or 5 days.

Visual exposure

Two animals in group K had the normal eye sutured at five weeks of age according to the methods of Wiesel and Hubel (1963). The remainder of the group K unilateral rotates were reared with both eyes open except for daily sessions of 3-5 hr of forced usage of the rotated eye. During these sessions vision through the normal eye was prevented by covering with a black contact occluder and kittens were kept alert and active to ensure adequate visual experience through their rotated eyes.

The two group A animals were also given several hours a day forced use of the rotated eye in the months after the operation and prior to testing.

Observation of visuomotor behavior

The visuomotor coordination of all our animals was observed repeatedly throughout development, but systematic testing was not begun until the kittens were capable of locomotion at 3-5 weeks of age. Black contact occluders were used to test the two eyes separately on a variety of tests for visuomotor behavior.

(1) Visual following with the head and body was tested with a v-shaped pointer light. The cats appeared to find this stimulus interesting and, unlike foil balls and moving fingers, the light was not associated with auditory or olfactory cues.

(2) Visual placing (triggered extension) was tested by slowly lowering the cat towards a broad surface; on control tests, the animal was carried in the same way but not brought close to a surface.

(3) Visually guided reaching was tested with an interrupted surface (Hein and Held, 1967). The animal was placed on a platform in front of the surface and the number of trials on which he reached directly and accurately for a prong, avoiding the gaps, was measured; on half of the trials, the animals faced a gap and had to reach to one side or the other to contact a prong. If the animals reached blindly they would have contacted the prong on about one-third of the presentations as the gap was twice as wide as the prong. Contacts with the side of a prong were scored as misses.

In addition, we informally observed the animals on an obstacle course and assessed jumping from various heights.

<u>Testing of visual discrimination</u>

Training was done in a modified Grice simultaneous two-choice discrimination apparatus (described by Myers, 1961), beginning when the animals were 3-4 months of age. For monocular training, black contact lenses were used to prevent vision through the unused eye. Double occluder tests (Ganz, Hirsch and Tieman, 1972) were run after the completion of each discrimination to ensure that the animals had not received any visual input through or around the occluders during training. Chance performance on these double occluder tests indicated that the lenses successfully blocked visual input.

Training consisted of discrete trials. To obtain food reward animals were required to walk down an alley and push open the correct one of two adjacent 10-12 cm translucent panels on which the stimuli were presented. The position of the positive stimulus varied according to Gellerman (1933) sequences. Cats were trained for approximately 40 trials per day until they reached a criterion of 90% correct responses for two consecutive days. Immediate correction of errors was permitted. After the first 40 trials position preferences, defined as 10 consecutive responses to one side, were broken by requiring a correct response to the nonpreferred side before advancing the sequence.

Prior to collecting the data reported here, all of the cats were pretrained (first binocularly and then with each eye separately) on one discrimination problem in order to adapt them to the apparatus and to ensure that they could learn under our testing conditions. The 2 group N cats and 15 of the 16 animals in group K were taught a pattern discrimination (□VS+) for pretraining. The last of the group

K animals (HCT) was taught a dark/light (brightness) discrimination. The group A cats were also pretrained on the brightness discrimination as we wished to test them at approximately the same age as cats in group K, and pattern discriminations take longer to learn than dark/light discriminations. The group A animals learned the brightness discrimination with both eyes open prior to surgery and then after 10 weeks experience with the rotation they relearned the problem to criterion with both eyes separately. Testing of the group A cats on the discriminations reported here began between 4 and 5 months after surgery.

Except for the pretraining problem, every cat learned each discrimination monocularly and was then tested for transfer to the other eye. Each cat learned half of the problems with one eye (rotated or normal) first and the other half with the other eye first. The order of testing the eyes was alternated across problems.

The stimuli for the brightness discrimination were transilluminated panels of which the average luminance measured 2.5 cd/ft^2 and 0.1 cd/ft^2. The pattern stimuli were high-contrast black outline patterns on a white background (average luminance 2.5 cd/ft^2). Cats rarely showed an initial preference for any of the stimuli but if a given cat did show a preference, it was trained against its preference.

For each problem three measures of interocular transfer were calculated: (1) change in initial performance (ΔI), which is the difference in the per cent of correct response during the first day (40 trials) of training for the first and second eyes; (2) trials analysis of per cent savings (% S_T), which is the ratio (a-b/a+b) (100) (a is the number of trials to criterion for the first eye and b for the second eye); and (3) errors analysis of per cent savings (% S_E), which is the above ratio with a and b indicating the errors to criterion with the 2 eyes. The trials and errors analyses usually agreed closely, but the latter measures have been emphasized because error analysis has the advantage of being a more faithful performance measure whenever a plateau occurs in the learning curve.

Measurement of the angle of rotation

We assumed that, prior to rotation, the fissured pupils were symmetrical. We measured the difference in the angle of the slit pupils from photographs of the eyes, which were taken with the cat awake and alert. Independent measurements of a given photograph differed by no more than ±2°, but different photographs of the same cat could yield estimates which differed by ±5° (cf. Nelson, Kado and Bishop, 1977).

Histology

In order to determine whether the rotations actually disturb normal retinal function (while also not wishing to sacrifice the cats which were being trained for these behavioral experiments), we prepared four other animals with large monocular rotations at the same age (7-10 days) and raised them in the same environment for histological purposes. As adults these animals were sacrificed 14 hr after an injection of 250 μC tritiated proline in 0.05 μl saline into the posterior chamber of their rotated eye. The cats were given an overdose of Nembutal and then perfused through the heart with isotonic saline followed by 10% formal/saline. The areas of the brain containing the dorsal lateral geniculate nucleus (dLGN) and superior colliculus (SC) were blocked and then sectioned at 40 μm intervals on a freezing microtome. After mounting on slides, the sections were prepared for autoradiography. They were dipped in photographic emulsion (Kodak NTB 2) and then exposed for about 4 weeks after which they were developed and then counterstained with cresyl violet and examined under light- and dark-field microscopes.

Whole mounts were made of the retinas from seven animals with large rotations. After perfusion the retinas were removed from the pigment epithelium by gentle teasing with forceps, placed on a slide and air dried and later stained with cresyl violet and examined under a light-field microscope.

Results

Histology

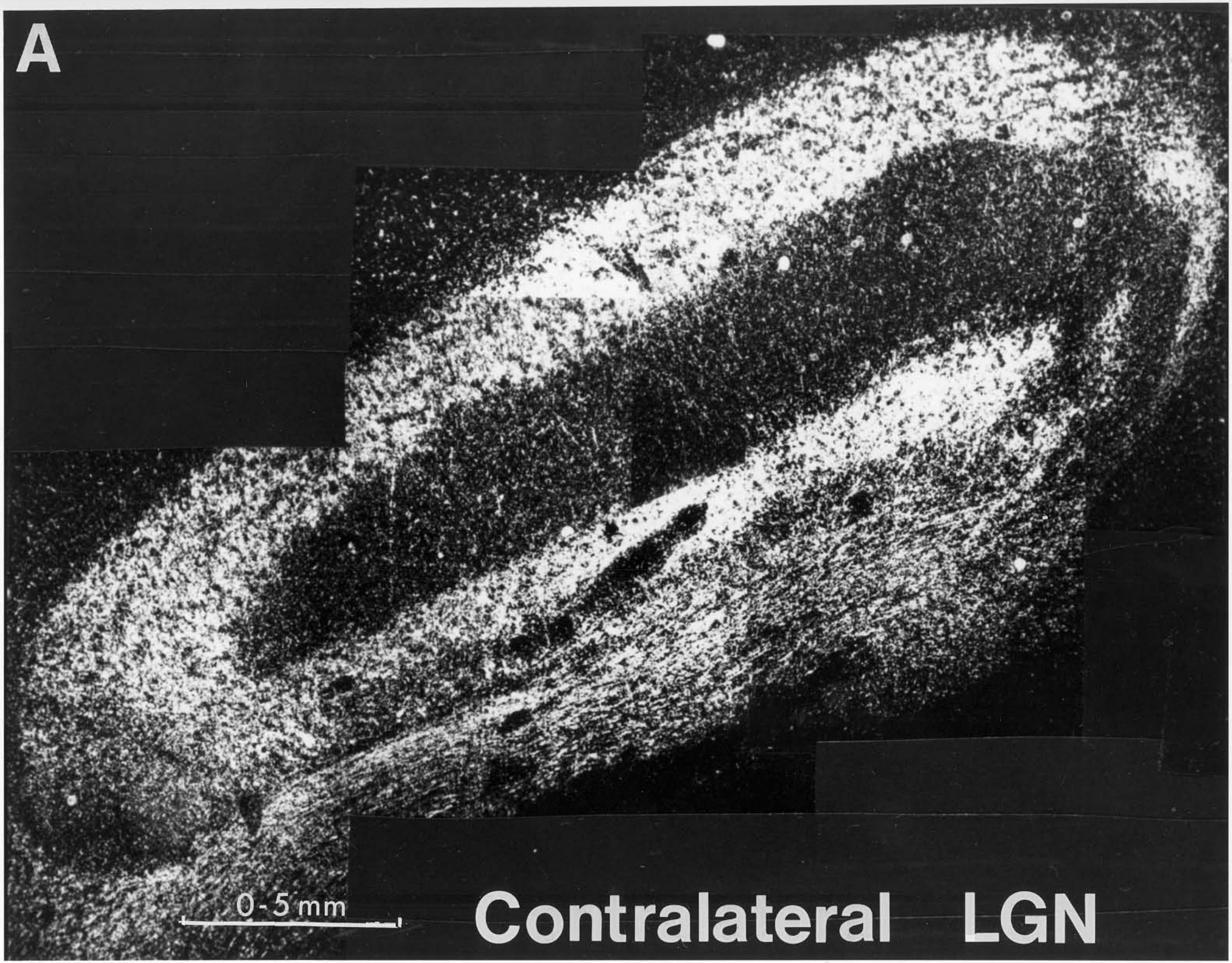
Whole mounts of the retinas of the rotated eyes of seven animals with large rotations did not show any obvious areas of cell damage or significant reduction in ganglion cell density. Examination of the LGN and SC of the animals injected with ^{3}H proline did not reveal any areas to which amino acid transfer from the retina was restricted. Fig. 1 shows representative coronal sections of the mid-region of the dLGN of an animal with an 180^o rotation after such an injection.

Visuomotor behavior

When tested monocularly with either eye, all of the cats in groups N, K, and A, including those with the largest (180^o) rotations, used their heads to follow accurately a moving stimulus in the absence of any auditory, olfactory, or somatosensory cues. A few animals oriented and followed less readily when tested with the rotated eye than when tested with the normal eye and one of the cats (HRC, in which both eyes were rotated) "lost" moving stimuli more readily under binocular viewing than under monocular viewing. None of the cats ever showed systematic mislocalization of the stimulus (cf. Sperry, 1943).

When tested with either eye open, all cats readily showed visual placing (triggered extension) when lowered toward a broad surface. This response was rarely observed when animals were similarly lowered in the absence of a surface. Visually guided reaching to a prong board was also positive. In Fig. 2, the results

Fig. 1 shows representative coronal sections through the midregion of the dorsal-lateral geniculate nucleus of an animal with a monocular rotation of 180° whose rotated eye was injected with 250 µC of ^{3}H proline 14 hr prior to sacrifice. A and B are contralateral and ipsilateral sections respectively. The grain density appears to be fairly uniform throughout the section suggesting that amino acid transport from the entire retina is fairly normal even in animals with the largest rotations.


A
Contralateral LGN
0·5 mm

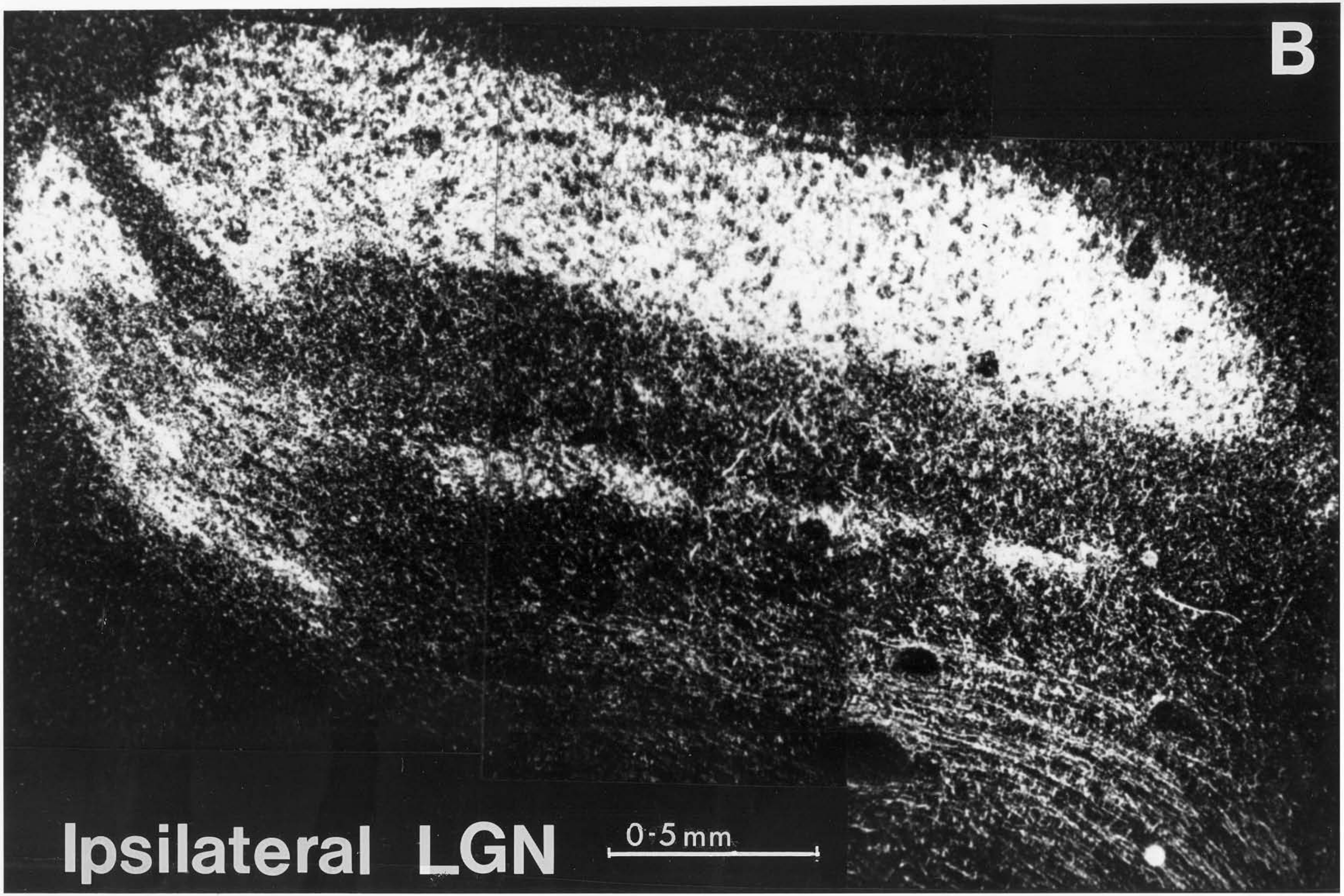
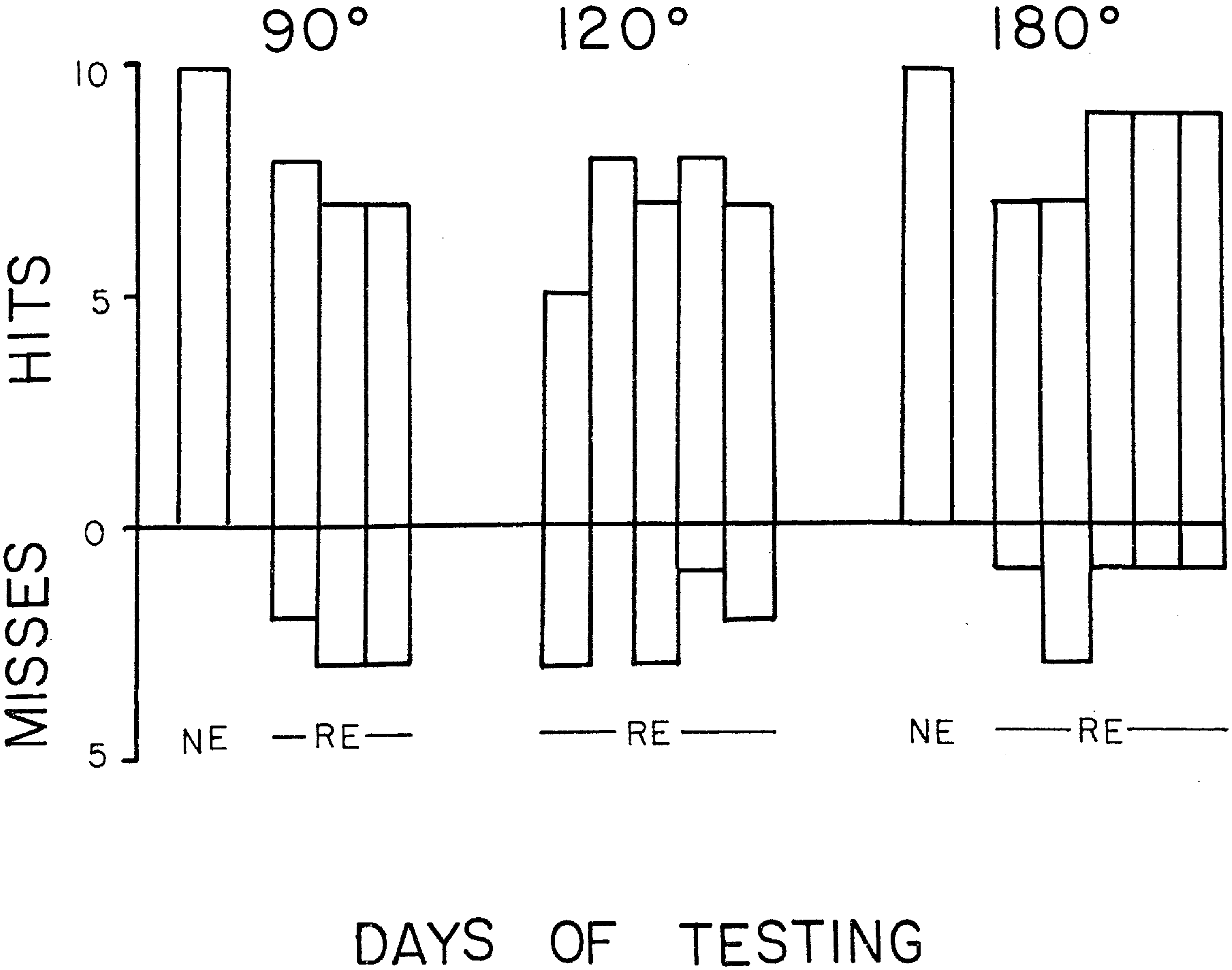

B
Ipsilateral LGN
0·5 mm

Fig. 2. Performance of 3 animals with large monocular rotations on repeated tests of visually guided reaching (i.e., visual placing using an interrupted surface). In each block of 10 daily trials the number of extensions of the forelimbs which squarely contacted a solid prong was indicated as number of 'hits' while the number of extensions towards a gap between prongs counted as misses for each animal whether using the normal eye (N) or rotated eye (R). The particular angle of monocular rotation for each of the animals is shown at the top of each series of tests.


90°
120°
180°
HITS
MISSES
10
5
0
5
NE
—RE—
——RE——
NE
——RE——
DAYS OF TESTING

of a series of repeated tests of visually guided reaching are shown for 3 animals with very large unilateral rotations (90°, 120°, and 180°). The animals were 4-5 months old at the time of these tests. With one exception (GEN on the first day of testing), each animal reached accurately for the prong on at least 70% of the presentations for each of the daily sessions. Chance was about 33%. There was very little variability in performance from day to day, and no tendency for the animal with largest rotation to perform worse than its littermates. The performance of the rotated eye, though good, was quantitatively inferior to that of the normal eye. (Only one day's results are shown, but we have repeatedly observed that normal animals show an extremely low rate of "misses" in this situation.)

When tested for obstacle avoidance in unfamiliar environments (cf. van Hof-van Duin, 1976), the animals were also quite skillful with either eye open: they swerved or ducked in anticipation of objects even while running rapidly. Most of them showed "uncertain jumping" (van Hof-van Duin, 1976) when placed on surfaces more than about 80 cm above the floor but they jumped readily from heights of about 40 cm.

Rate of learning: brightness (flux) and pattern discriminations

The results of the tests for visual discriminations are shown in Tables I and II. All cats in group K except the 3 cats with the largest unilateral (180°) rotations learned each of the visual discriminations on which they were tested. The three cats with 180° rotations required more trials and made more errors on the dark/light problem than the other group K kittens. In general both the numbers of trials and errors to criterion tended to be greater when a problem was learned through the rotated eye rather than through the normal eye first. However, the average number of trials required by the cats learning first with

Table I

Trials to criterion for individual cats.

In the case of animals with unilateral rotations, whether groups K or A, E indicates learning of the discrimination through the rotated or experimental eye, N indicates learning through the normal eye, and B with both eyes open.

For the animals with binocular rotations R and L represent the right and left eyes respectively. NT indicates that an animal was not tested on a particular discrimination. The negative angle shown for bilateral rotation 15 indicates that the left eye was extorted rather than intorted as were all other rotations.

		CAT	ANGLE OF ROTATION	DISCRIMINATIONS			
				■ vs. □	☰ vs. ⫴	⧹⧹ vs. ⫽	▽ vs. △
GROUP K							
1. UNILATERAL ROTATION AT 8-10 DAYS							
NORMAL EYE CLOSED DURING REARING	1	AGR	10°	233 E, 199	235 E, 105	140 N, 101	627 E, 120
	2	AGS	55°	546 N, 50	271 N, 120	812 E 511	1501 N, 0
NORMAL EYE OPEN DURING REARING	3	DCN	10°	200 E, 80	507 E, 0	120 N, 401	N.T.
	4	ATL	30°	111 N, 0	222 N, 0	294 E, 26	368 N, 0
	5	AAG	40°	201 N, 0	165 E, 0	401 N, 240	280 E, 80
	6	ART	45°	293 E, 29	274 N, 130	808 E, 80	N.T.
	7	CSR	60°	310 N, 80	398 E, 216	187 N, 80	503 E, 201
	8	HCT	60°	190 B, 179 E, 0N	198 N, 0	269 E, 60	411 N, 112
	9	ARS	65°	160 E, 0	120 N, 105	605 E, 0	480 N, 120
	10	GEN	120°	1010 N, 652	912 E, 67	N.T.	N.T.
	11	GLL	180°	368 E, 120	> 1000 E		
	12	GTE	180°	374 E, 40	> 1000 E	Unable to learn pattern discrimination	
		HRN	180°	459 B	> 1000 E		
2. BILATERAL ROTATION AT 8-10 DAYS							
	13	HRC	70°L, 90°R	182 B, 25 L	341 L, 559	1874 R, 38	958 L, 160
	14	KLV	20°L, 80°R	500 L, N.T. R	233 R, 159	452 L, 71	1397 R, 196
	15	KSR	-50°L, 60°R	486 L, 167 R	178 R, 118 L	N.T.	N.T.
GROUP A							
UNILATERAL ROTATION AT 6 MONTHS							
		LAF	30°	——	1146 R, 25	227 N, 40	483 R, 120
		LNC	70°	——	285 N, 183	240 R, 92	339 N, 301
GROUP N							
NORMAL		PER	0°	80, 0	40, 0	120, 0	160, 0
		LEA	0°	51, 0	152, 0	461, 0	220, 0

Table II

Errors to Criterion for Individual Animals

(Abbreviations are the same as those in Table I)

		CAT	ANGLE OF ROTATION	DISCRIMINATIONS			
				■ vs. □	≡ vs. |||	⟍⟍⟍ vs. ///	▽ vs. △
GROUP K							
1. UNILATERAL ROTATION AT 8-10 DAYS							
NORMAL EYE CLOSED DURING REARING	1	AGR	10°	52 E, 57	86 E, 28	54 N, 22	230 E, 17
	2	AGS	55°	179 N, 20	122 N, 34	316 E, 126	494 N, 0
NORMAL EYE OPEN DURING REARING	3	DCN	10°	82 E, 14	178 E, 0	40 N, 80	N.T.
	4	ATL	30°	49 N, 0	61 N, 0	95 E, 3	164 N, 0
	5	AAG	40°	84 N, 0	56 E, 0	146 N, 74	107 E, 21
	6	ART	45°	115 E, 5	126 N, 28	290 E, 15	N.T.
	7	CSR	60°	111 N, 23	167 N, 40	81 E, 13	150 N, 49
	8	HCT	60°	93 B, 24 E, ON	59 N, 0	118 E, 12	171 N, 26
	9	ARS	65°	67 E, 0	40 N, 22	156 E, 0	150 N. 19
	10	GEN	120°	260 N, 260	297 E, 13	N.T.	N.T.
	11	GLL	180°	128 E, 27 N	Unable to learn pattern discrimination		
	12	GTE	180°	156 E, 18 N			
		HRN	180°	151 B			
2. BILATERAL ROTATION AT 8-10 DAYS							
	13	HRC	70°L, 90°R	57 B, 7 L	110 L, 175	824 R, 22	349 L, 36
	14	KLV	20°L, 80°R	177 L, N.T. R	98 R, 32	216 L, 12	504 L, 42
	15	KSR	-50°L, 60°R	167 L, 48 R	58 R, 27	N.T.	N.T.
GROUP A							
UNILATERAL ROTATION AT 6 MONTHS							
		LAF	30°	___	449 R, 8	110 N, 17	214 R, 26
		LNC	70°	___	97 N, 78	123 R, 18	116 N, 113
GROUP N							
NORMAL		PER	0°	40, 0	22, 0	39, 14	42, 0
		LEA	0°	16, 0	69, 0	160, 0	89, 0

the rotated eye was never more than twice as great as the average of cats learning the same problem with the normal eye. In fact, on both the dark/light and the inverted triangle discriminations, the mean number of trials was almost identical for the two groups, but on the discriminations of oriented lines (||| vs. ≡ and \\\ vs. ///), the rotated eye generally showed more prolonged learning, although there was considerable overlapping of ranges of trials for the two eyes. It is important to note that, because of the alternate order of testing of the two eyes, if a given cat was taught the horizontal/vertical discrimination with its normal eye first, it was taught the discrimination between diagonal lines with the rotated eye first, so that the overall ability of a given animal was balanced across problems. In comparison to the 2 normally-reared kittens (group N), both the normal and the rotated eyes of group K animals showed prolonged learning on all problems but one (diagonal lines); the reason for this is not clear.

Neither bilateral rotation nor suturing the lids of the normal eye led to a marked improvement in the rate with which group K animals learned visual discriminations with the rotated eye. Surprisingly, 2 of the 3 animals with bilateral rotations (HRC and KLV) had considerable difficulty learning with one eye (see Table I), although in the case of KLV the horizontal/vertical line discrimination was learned at a reasonable rate with the affected eye.

The two animals with unilateral rotations as adults (group A) learned all of the problems at rates roughly comparable to those of the group K animals with unilateral rotations with only one exception (see Table I): LAF required over 1000 trials to learn the horizontal/vertical discrimination with her rotated eye. This may be attributable to her learning history. She had not previously learned a pattern discrimination.

The difference in discrimination learning between the cats with 180° unilateral rotations and the cats with smaller binocular rotations of about the same total angle is exemplified in Fig. 3, which shows learning curves for 2 of the cats (HRC and HRN). HRC and HRN were both male cats and littermates; the data shown were collected 12-15 months after surgery. HRN had one eye intorted 180°, and was unable to learn even the simplest pattern discrimination (||| vs. ≡) with the rotated eye, although he learned normally with the unrotated eye. In contrast, HRC had both eyes intorted, 70° and 90°, for an interocular difference of 160° and he learned ∇ vs. Δ (a much more difficult discrimination) with one eye and showed substantial transfer of the information to the naive eye.

Interocular transfer of brightness and pattern discrimination

As expected, the normal cats required little or no further practice to perform a discrimination with the second naive eye after having learned the same problem with one eye (see Tables I and II). Cats in both groups A and K also performed significantly above chance on the first 40 trials (ΔI) with the naive eye after learning the same discrimination with the other eye (Fig. 4). These cats also showed considerable, though not complete, transfer on all the discriminations, as judged by analysis of savings (Fig. 5). The 2 animals of group K in which the normal eye had been closed during development tended to show less transfer than the other unilateral rotates. The adult rotates showed transfer quite comparable to that of kitten rotates. Neither the mean nor the variability of this transfer differed significantly from that shown by the animals of group K. Similarly, the 3 cats with bilateral rotations did not show significantly different transfer of the discriminations than did cats with unilateral rotations.

Fig. 3. The learning curves for two animals, HRN (with a unilateral rotation of 180°) and HRC (with a combined angle of rotation of 160° after binocular rotation), are shown in terms of per cent of trials correct each day for two discrimination problems. HRN's performance on the simplest orientation problem never reached criterion (90% correct in two consecutive days) with the rotated eye (R), although criterion was achieved quite rapidly when the animal was trained through the normal eye (N). By comparison HRC, which had bilateral rotations of approximately the same total angle, was able to learn the most difficult problem (▽ *vs.* △) and show transfer from the left eye LE to the right eye RE. Chance performance was 50% correct.

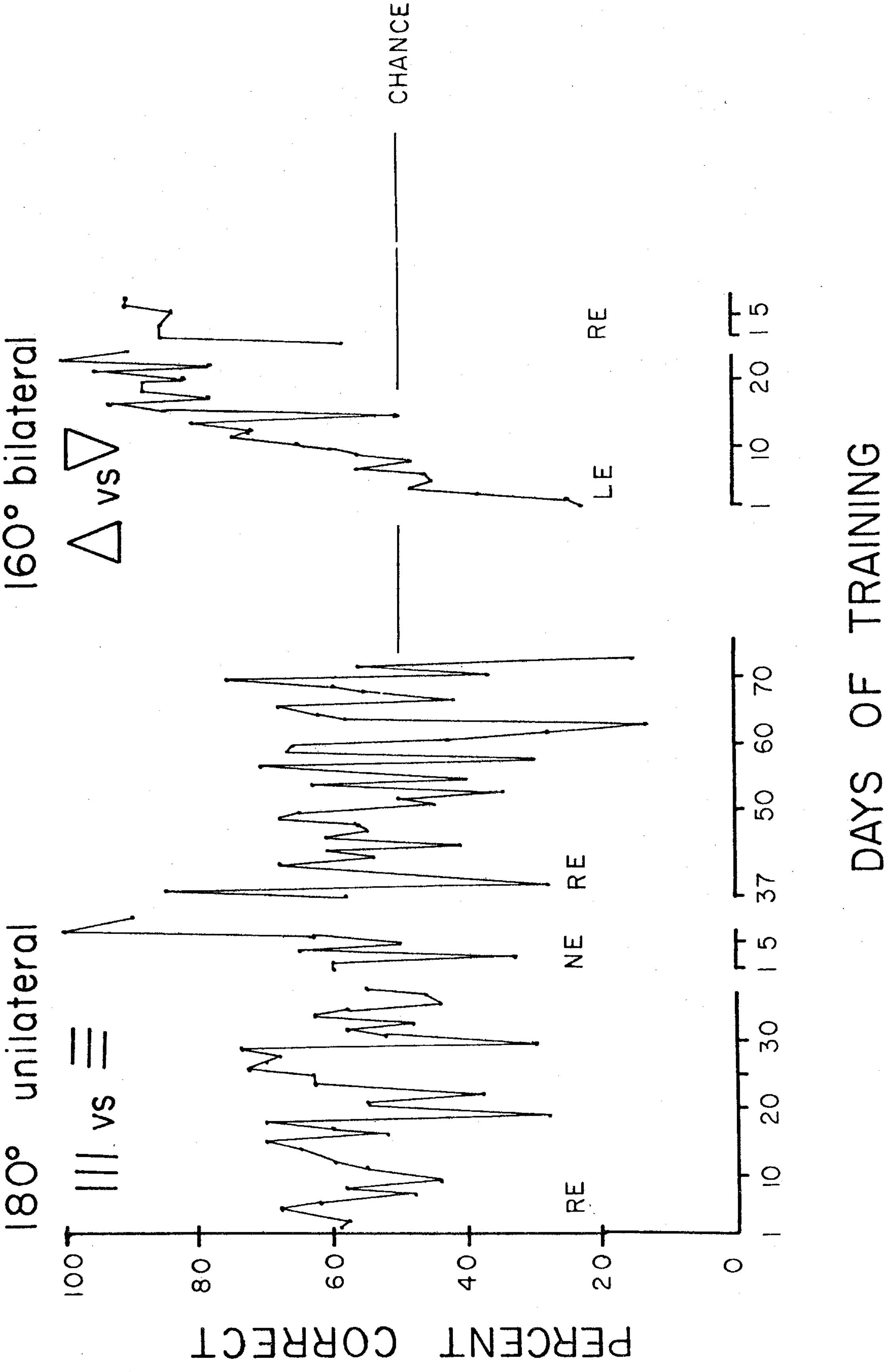

180° unilateral
||| vs ≡
160° bilateral
△ vs ▽
PERCENT CORRECT
100
80
60
40
20
0
RE
NE
RE
LE
RE
CHANCE
1
10
20
30
1
5
37
50
60
70
1
10
20
1
5
DAYS OF TRAINING

Fig. 4. Initial performance Δ I (per cent correct responses during the first 40 trials of testing) for the first and second eyes of individual cats as a function of the angular difference in rotation of the two eyes. The numbers permit cross-reference to Tables I and II. The per cent correct for the first 40 trials with the first eye is indicated by the horizontal base of the bars. The length of the vertical line represents the change in initial performance for all animals. The initial performance for the second eye and the order of training for animals with monocular rotation is indicated by a triangle (Δ) where training was through the normal eye first and by a circle (O) where training was through the rotated eye first. A square ( ) and a cross (X) show the initial performance of the second eye of animals with binocular rotations and rotations as adults respectively. Closed symbols indicate the 2 animals whose normal eyes were sutured during the critical period.

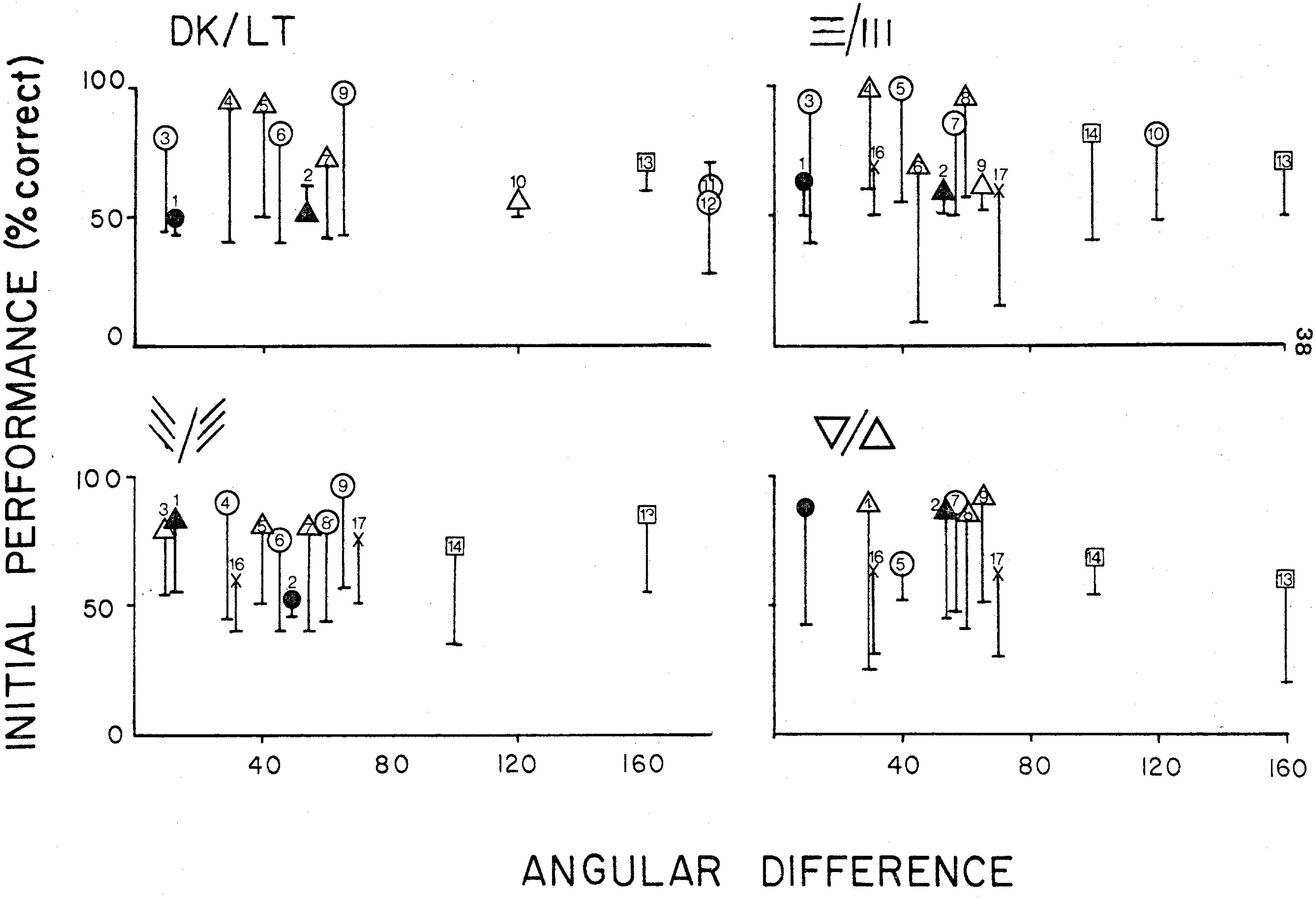
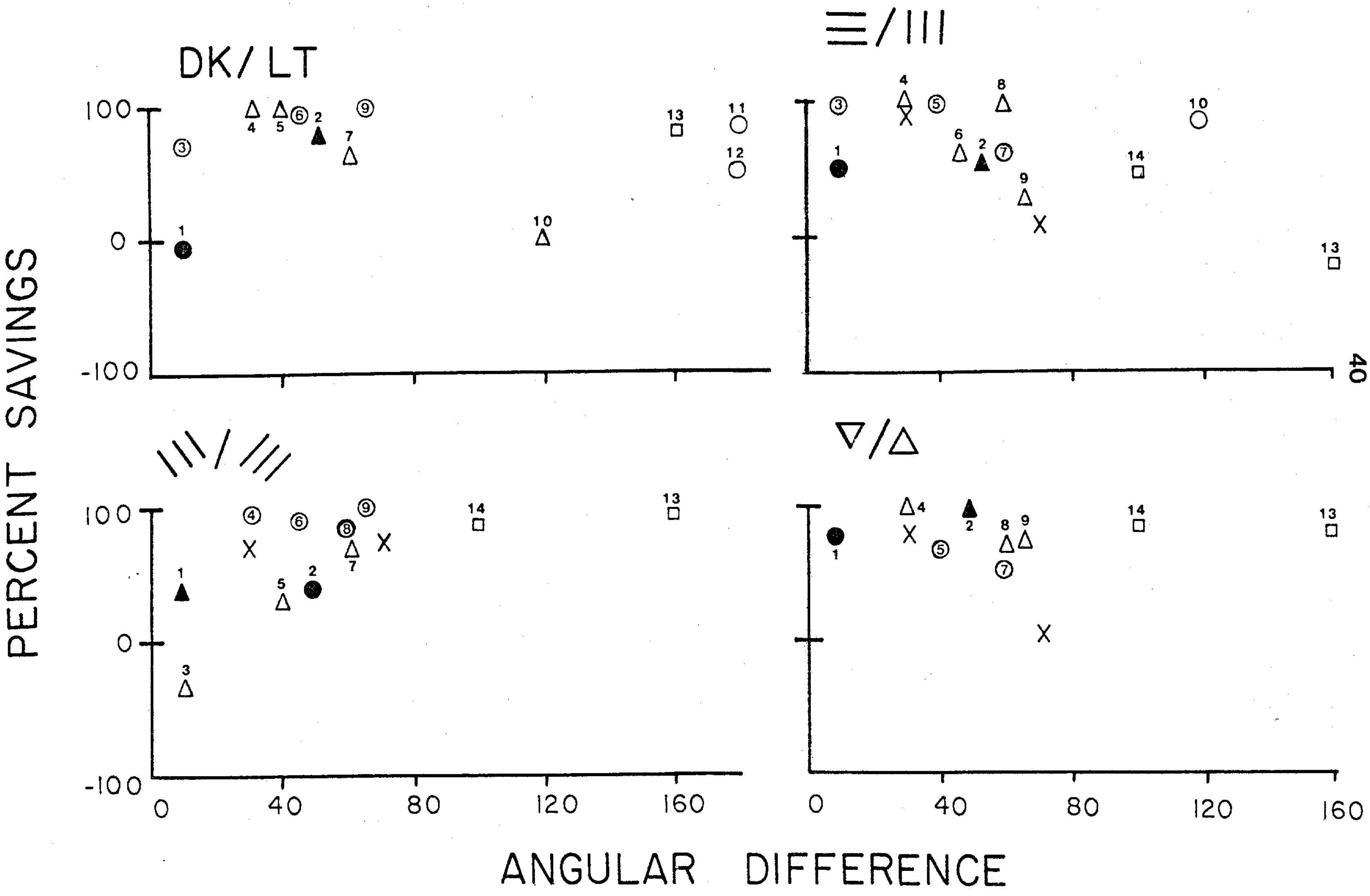

DK/LT
∇/Δ
INITIAL PERFORMANCE (% correct)
100
50
0
40
80
120
160
ANGULAR DIFFERENCE
1
2
3
4
5
6
7
8
9
10
11
12
13
14
16
17

Fig. 5. Interocular transfer of learned discriminations for each cat is shown in terms of errors analysis of per cent savings where the per cent savings (% S_R) is calculated from the ratio (a-b/a+b) (100) where a is the number of errors to criterion for the first eye and b is the number of errors to criterion for the second eye. A circle (O) represents interocular transfer of savings from the rotated eye to the normal and a triangle (Δ) represents the transfer of savings from the normal eye to the rotated eye. Animals with binocular rotations are indicated by a square ( ) and adult rotations are identified with a cross (X). Closed symbols again indicate the 2 animals in group K raised throughout the critical period with monocular suture of the normal eye. Again the numbered position of each symbol along the horizontal axes indicates the rotation disparity between the two eyes and identifies the animals with the information in Tables I and II. Table II contains all the raw data.


DK/LT
≡/|||
\\\////
∇/Δ
PERCENT SAVINGS
ANGULAR DIFFERENCE
100
0
-100
0
40
80
120
160
1
2
3
4
5
6
7
8
9
10
11
12
13
14

Most cats showed substantial transfer of brightness discrimination, although it is puzzling that low levels of transfer were seen in the two cats with the smallest rotations. There was no consistent decline in transfer of discriminations of orthogonal lines (horizontal vs. vertical, and diagonal lines 45° vs. 135°) as a function of angle of rotation, with the possible exception of one cat. AGS, who showed less transfer on either of these problems than on the brightness or inverted triangle/ discrimination. Other cats, such as AAG and ARS, showed less transfer on one of the orthogonal-line discriminations than on the other, and intermediate levels of transfer on the triangle discrimination.

Some of the variability for a given cat on different problems might be thought to be due to the alternate order of testing the eyes. If animals simply learn faster with the normal eye than with the rotated eye, because of some variable such as acuity within the rotated eye, then a savings measure confounds perceptual transfer with speed of learning. In Fig. 5, we have used different symbols to indicate transfer of saving from the rotated eye to the normal eye (circles) and from the normal eye to the rotated eye (triangles). In general, transfer from the rotated eye to the normal eye does not seem to be superior. Also, initial performance measures of transfer which would be largely uninfluenced by speed of learning usually corresponded quite closely to the savings measures. Fig. 4 shows the initial performance measures for both eyes as bar graphs using the same conventions as in Fig. 5.

Discussion

Two major issues concerning behavioral plasticity are addressed in this paper. The first concerns the visuospatial capacities of animals with various angles of rotation up to 180° between the two eyes. We have used several testing procedures to assess the degree of visuomotor adaptation of adult cats and of kittens raised from infancy with differential rotation of the visual fields to the two eyes. Secondly, we have examined the ability of these animals to learn two choice discriminations of oriented patterns and then to transfer such information interocularly.

Visuomotor adaptation

Many examples of good behavioral compensation for geometrical displacements of the visual field have been reported for primates (review, Welch, 1974); however, there has been relatively little investigation of the visuomotor capacities of any other mammalian species following either surgical or prismatic rotation. Good visually-guided behavior was shown by all of our animals--including those with unilateral rotations of 180° and those with binocular rotations of 80° in each eye--when using only a rotated eye regardless of whether the operation was performed at the time of eye-opening or after the critical period for binocular visual development (Hubel and Wiesel, 1963, 1970; Blakemore and Van Sluyters, 1974). Good visuomotor behavior persisted even when the animals were placed in an unfamiliar environment (van Hof-van Duin, 1976). These observations confirm and extend the earlier reports of Blakemore *et al.* (1975), Mitchell *et al.* (1976), and Peck and Crewther (1975), and contrast with the studies of Yinon (1975, 1976, 1977) in which severely disturbed visuomotor behavior following surgical rotation of one eye in infancy or in adulthood was found.

Even though our animals showed good visuomotor behavior on a variety of tasks, when the performance of visually-guided reaching was measured with an interrupted surface the performance of the rotated eye was quantitatively inferior to that of the normal eye. We do not know whether these results might be limited by differences in acuity between the two eyes, as our tests of the relative acuity of the two eyes are incomplete. However, these data on visually-guided reaching seem to suggest that, although visuomotor adaptation to the rotationally disparate visual information has occurred, such adaptation is not complete even when the rotation is induced in infancy.

Bishop (1959) also reported considerable adaptation in kittens which were given several weeks of visual experience with inverting prisms. However, Bishop noted that the performance of the kittens on several visuomotor tasks, although creditable, was not as good as that of a control group of animals who did not wear prisms. Both normal (Foley, 1940; Hamilton, 1967) and split-brain monkeys (Bossom and Hamilton, 1963; Hamilton, 1967) have also been reported to show good visuomotor adaptation while wearing laterally displacing prisms. In contrast, there are varied reports about adaptation to prism-induced pecking errors in young chicks (Hess, 1956; Rossi, 1968), while there appears to be no evidence of behavioral compensation for visual field rotation in amphibians (Sperry, 1943; Stone, 1940) and fish (Sperry, 1948).

Learning of brightness and pattern discriminations

Theories of visuomotor adaptation (reviewed by Harris, 1965; Howard and Templeton, 1966; Welch, 1974) would all predict that, once adapted, animals should be able to learn pattern discriminations when using visual information which was either optically or surgically displaced, provided the procedure did not damage the eye itself or severely degrade the retinal image. We have thus examined the ability of kittens raised with either a rotation of one or both eyes (group K) and of adult cats (group A) whose rotation was produced after the critical period to learn a standard series of visual two choice discriminations with the rotated eye. All animals in groups K and A with unilateral rotations up to 120° or bilateral rotations with a total angle of 160° between the visual axes were able to learn each of the brightness and pattern discriminations with the rotated eye open and the normal eye occluded. The learning rate tended to be slower when cats were trained through the rotated eye first, in comparison to those trained with the normal eye first. However, the average number of trials when learning through the rotated eye was never more than twice that of the normal eye. These results confirm and extend our earlier findings (Peck and Crewther, 1975) and those of Mitchell *et al.* (1976) for cats with smaller rotations and further suggest that the animals have at least reasonable acuity with the rotated eye.

The three animals with 180° rotations were able to learn brightness but not pattern discriminations (see Table I). We do not know whether this is a function of some damage produced by the surgical inversion or whether it reflects an inability to deal with the inverted visual information; the visuomotor behavior and the histological results would seem to rule out any explanation based on gross damage to the eye or the visual pathways.

Interocular transfer of brightness and pattern discrimination

If visuomotor adaptation occurs after surgical rotation of an eye it is of interest to theories of perception to consider whether animals really see objects in space as identical or equivalent when viewed normally through one eye and rotationally (or laterally) displaced through the other eye, or whether the information is interpreted differently by the two eyes. We have attempted to assess these effects by determining the degree of interocular transfer as measured by the differences in initial performance of the two eyes ΔI or by the percentage savings in errors or trials to criterion.

Animals in both groups K and A showed considerable but not complete interocular transfer for both measures of transfer on all discriminations. There was a tendency for cats in group A to show slightly less transfer than those in group K although it would be necessary to test a larger group of adult rotates to determine the reliability of this difference.

Partial interocular transfer can be interpreted in several ways. It is possible that in addition to showing behavioral adaptation in tests of visuomotor coordination, an actual perceptual reorientation to the rearranged visual information may have occurred. This would lead to equivalent visual perceptions through the normal and the rotated eye resulting in veridical interocular transfer. Alternatively, visual perception may not have adapted in the sense of a compensatory rotation of the visual field but the animals may have learned the orientation discriminations in terms of the alignment of the stimuli relative to other objects in the visual field, all of which might still appear rotated. It also is possible that appropriate behavior contingent on which eye was being used could have been learned by the animal even though no perceptual adaptation per se had occurred. Thus despite our observation that the rotated eyes perform well on visual tasks and the large increases in initial performance of the second eye seem to indicate that the normal and rotated eyes show some behavioral equivalence in recognizing the same visual stimulus, it is probably unwise to conclude that significant levels of interocular transfer directly indicate that the animals have readjusted their visual processing of patterned stimuli.

One might expect that, to the degree that compensation for the rotation is incomplete, the amount of transfer shown on patterns of varying orientation would vary with the angle of rotation of the eye. We did not "tailor" individual orientation problems to the particular angle of rotation for each animal, rather each cat was taught a "standard" set of discriminations to allow comparison of systematic increases and decreases in the amount of transfer as a function of angle. However as shown in Fig. 4 there did not appear to be any significant correlation between the angle of rotation and the degree of interocular transfer.

Mechanism and locus of adaptation

Neither the mechanisms nor the loci of central nervous system involvement in visuomotor adaptation and in interocular transfer of oriented pattern discrimination are immediately obvious. The large literature dealing with prism rotations, inversions, and distortions has suggested many hypotheses which have been reviewed by Harris (1965), Howard and Templeton (1966), and Welch (1974). The most important theories consider adaptation to be either a process of a visuomotor recorrelation (Held, 1961), a change in the position sense of the body (Harris, 1965), or a change in the motor system (Snyder and Pronko, 1952) or in the visual system itself.

More recently most authors have argued that there is no adjustment within the visual system itself, but that all adaptation involves changes, recalibrations or reinterpretations of the position sense of various parts of the body (Hamilton, 1967; Harris, 1965; Welch, 1974). In one of the most direct tests of the idea of positional or proprioceptive change, split-brain monkeys as well as normal monkeys showed interocular transfer of prism-altered visually directed reaching although the same monkeys did not show intermanual transfer of adaptation to the same task (Hamilton, 1967). In contrast, visual learning of pattern does not transfer interocularly in split-brain monkeys (e.g., Sperry, 1961). Lastly because severing the cerebral commissures did not prevent the split-brain monkeys from showing adaptation of directed reaching it is proposed that adaptation either occurs subcortically or utilizes subcortical mechanisms.

Visual changes per se have been postulated by other workers to be important for visuomotor adaptation (Kohler, 1964; Taylor, 1962). However the visuomotor behavior and interocular transfer of pattern discriminations seen in our group A cats whose eyes were rotated after the critical period for physiological alterations in primary visual cortex (Blakemore and Van Sluyters, 1974; Hubel and Wiesel, 1970), would suggest that adaptation does not produce a physiological change analogous to that seen in experiments with selective rearing such as monocular deprivation (Wiesel and Hubel, 1963) or stripe raising (Hirsch and Spinelli, 1971). Direct electrophysiological examination of the visual cortex of animals raised with disparate visual information to the two eyes has yielded mixed results concerning the extent of the plasticity to be seen in neuronal properties. Shinkman and Bruce (1977) have studied the preferred orientations of neurons in area 17 of kittens whose total visual experience was through binocular prisms which rotated the visual world through 8^o (for a total difference of 16^o between the inputs of the two eyes), and reported that the orientation disparity of the cells had changed to about the same degree. On the other hand, the initial physiological studies of striate cortex of cats with unilateral surgical rotation showed none of the plastic changes in the cortex which could account for adaptation. Neither Blakemore et al. (1975) nor Yinon (1975) found any apparent adaptation of the preferred orientation of binocular cells which would explain the perceptual equivalence which is indicated by the high level of interocular transfer shown by our cats. Our own preliminary unpublished results however suggest that adaptation may elicit some changes in the preferred direction of movement of layer V corticotectal cells of animals given rotations as kittens. These cells are relatively insensitive to the orientation of a stimulus and respond as well to movement of a spot in a preferred direction as to a bar (Palmer and Rosenquist, 1974). In the case of several of our animals with large monocular rotations it has been possible to record significant shifts in the direction preference of some of these cells. Such a shift in direction preference might contribute to the accurate and rapid visuomotor responses we observed in our animals.

The high level of interocular transfer reported here and the low level of binocularity observed by Blakemore et al. (1975), Yinon (1975), and by Crewther, Crewther and Peck in Chapter III also argue against the necessity of a large proportion of finely tuned binocular neurons at the level of area 17 for interocular transfer of pattern discrimination learning. The literature on the effects of discrete cortical lesions in cats also appears to support a similar conclusion (Bauman and Spear, 1977; Doty, 1971; Sprague, Levy, Di Bernadino and Berlucci, 1977; Winans, 1971).

In conclusion, all of our animals, including those with monocular rotations up to 180^o and binocular rotations of up to 90^o in each eye, showed good visuomotor behavior when using the rotated eye. Kitten rotates and adult rotates showed comparable visuomotor adaptation. Although the rotated eye learned somewhat more slowly than the normal eye, all animals except those with monocular rotations of 180^o were able to learn several two-choice pattern discrimination problems and showed considerable interocular transfer of such information. The three animals with the 180^o rotations were able to learn brightness discriminations and transfer that information interocularly.

CHAPTER III

Comparison of the Effects of Monocular and Binocular Rotation on the Physiology of Area 17 in Cats

Introduction

Selective alteration of the early visual environment has proved to be a useful tool for the investigation of plasticity in the visual system. For instance, when kittens are reared with artificial strabismus produced by surgical section of an extraocular muscle, very few neurons of the visual cortex can be activated by both eyes (Hubel and Wiesel, 1965). This contrasts with the situation in normal animals where most of the cortical cells can be driven by the two eyes (Hubel and Wiesel, 1962). Psychophysical studies in humans also indicate that binocular interaction is absent if the visual axes of the two eyes are incorrectly aligned during childhood (Banks, Aslin and Letson, 1975; Mitchell and Ware, 1974; Movshon, Chambers and Blakemore, 1972). It is commonly thought that such deficits in binocular vision are the result of the inability of cortical neurons to receive or maintain disparate visual inputs from the two eyes (e.g., Hubel and Wiesel, 1965; Stent, 1973). By contrast, Maffei and Bisti (1976) have recently reported that the ocular dominance distribution of cortical neurons in strabismic kittens is skewed towards monocular even when the animals are reared in the dark and have suggested that factors other than asynchronous visual information are also important. Maffei and Bisti interpreted their results as evidence that asymmetrical eye movements are sufficient to affect binocular interaction within the visual cortex. However, there are at least three consequences of cutting the extraocular muscles: the eyes are misaligned, normal eye movements are disrupted and the positional information from the extraocular muscles is disturbed at least for the short time while the muscles are reattaching.

In the present experiment, we tested the effects of incongruent visual experience and nonconjugate eye movements on cortical physiology in two groups of cats reared with large angular divergences between the two visual axes and with asymmetrical eye movements. All animals were given either monocular or binocular rotations at the time of natural eye opening and were then used for behavioral studies examining the plasticity of visuomotor coordination and perceptual capacities after rotation of the visual field (Chapters I and II). On completion of these studies the two groups of animals were prepared for visual cortex electrophysiology. It is already known from previous studies (Blakemore, Van Sluyters, Peck and Hein, 1975; Yinon, 1975) that monocular rotation during the critical period reduces binocularity. However, this manipulation is only done to one eye and a recent experiment of Maffei and Fiorentini (1976) has suggested that monocular paralysis has more drastic effects than binocular paralysis on adult ocular dominance. We decided therefore, to compare the effects of unilateral rotation on cortical ocular dominance with the effects after bilateral rotation. Surprisingly, recordings from area 17 following binocular rotation demonstrated that most neurons could be activated by both eyes thus indicating that incongruent visual input to the two eyes does not by itself necessarily lead to a loss of binocularity. In addition, since both groups of cats have many nonconjugate eye movements it seems unlikely that the asymmetrical eye movements necessarily affect cortical binocularity.

Physiological examination of the properties of individual neurons indicated that some plastic changes in direction preference occurred in the layer

V corticotectal cells in animals from both experimental groups with a total rotation angle of around 90°.

Methods

Animals and rearing conditions

19 kittens were used in this experiment. All were born in our closed laboratory colony, and lived with their mothers and littermates in large pens until after weaning. At around 3-4 months they were transferred to a large colony room for individual housing in standard sized cages. The room was illuminated for around 12 hr each day.

Two of the kittens were given normal visual experience in the same environment (group N). Ten (group MR) animals were given different angles of monocular intorsion ranging from 3°-200° from the original orientation of the eyeball at the time of natural eye opening (7-10 days). Of these, two animals MR1 and MR10 had the normal eye sutured from 5 and 3 weeks to 14 weeks respectively. MR3 was given an extorsion of 10°. Eight kittens were given binocular rotations at 7-10 days (group BR). Seven of these animals had both eyes intorted; one had the left eye intorted and the right eye extorted. Fig. 1 shows what animals from both experimental groups looked like after surgical rotation of one or two eyes.

Six of the kittens with monocular rotations were also used in the behavioral experiments (Chapter II) and were given extensive experience using the rotated eye during the critical period. Each of these animals had a black contact occluder placed in its normal eye for several hours each day and was allowed to scamper around the exercise pens. An effort was made to ensure that the animals actually used the rotated eye for most of this time.

Fig. 1. Photographs of animals with surgically induced intorsions of the eyes.

A. Photograph of an animal with a monocular rotation of 90°.

B. Photograph of an animal with binocular rotations. In the normal cat the fissured pupils appear almost vertical.

A

B

Tables I and II show all pertinent details of animals including angles of rotation and age at the time of recording. The angles of rotation were measured from photographs of the fissured pupils taken in bright light. This method was reliable to within a couple of degrees which was deemed sufficiently accurate as most of the rotations involved were large.

Surgery and preparation for recording

Animals were prepared for surgical rotations either by sedating with 0.2 cc Equithesin followed by fluothane anesthesia, or by exposure to a gas mixture of 1-2% fluothane in N_2O/O_2 (2:1).

The methods of rotation have been described more fully elsewhere (Chapter II). Briefly the conjunctiva was dissected away from the eyeball, and then the muscles were caught with a blunt hook and cut near the point of tendon insertion on the globe. When all the muscles had been detached the eyeball was quite easy to rotate around the optic disc and showed little tendency to revert to its original position. An attempt was made to prevent any large deviation from the original optic axis. The angle of rotation was estimated either from the angle of the pupillary fissure or from the position of the superior opthalmic vein. A few drops of broad spectrum opthalmic antibiotic for a few days post-surgically insured that healing proceeded rapidly. Eye movements were not usually seen until around 6-8 days later in both experimental groups.

The method of preparation for electrophysiological recording has been described in Crewther, Crewther and Pettigrew (J. Physiol., in press) and others. The tracheotomy and cephalic vein cannulation were performed under an anesthesia mixture of 1-2% fluothane in 2:1 $N_2O:O_2$. Cats were then transferred to the stereotaxic apparatus and paralyzed with an intravenous (i.v.) injection of 40 mg

TABLE I

Cat	R #	Age at Recording	Angle of Rotation Before Flaxedil	Angle of Rotation After Flaxedil	Preferred Orient. Disparity (degrees)	Standard Deviation (degrees)	Mean Orientation Tuning (degrees)	
							IPSI	CONTRA
AGR	MR1	19 mo.	7	10	2	11	-	-
ATT	MR2	19 mo.	25	35	15	25	62±22	56±22
MIL	MR3	3½ mo.	-10	-8	-6	22	61±30	65±25
MAC	MR4	4 mo.	57	63	78	38	74±28	89±44
NIC	MR5	4 mo.	95	99	73	17	65±17	59±26
GEN	MR6	20 mo.	108	119	21	64	126±43	121±48
ZAC	MR7	10 mo.	70	80	78	13	73±33	76±34
GAR	MR8	29 mo.	90	94	97	7	83±41	103±46
AAG	MR9	36 mo.	40	45	30	24	57±7	68±9
KAT	MR10	24 mo.	196	200	197	37	151±45	151±45
MAI	MR11	12 mo.	5	5	18	45	71±16	74±18

TABLE II

Cat	R #	Age at Recording	Angle of Rotation		Angle of Rotation Under Flaxedil	Mean Orient Disparity of Binocular Neurons Δ	Standard Deviation σ_Δ	Percent Direction Selective	Mean Orient. Tuning Width $\overline{T}$	Standard Deviation σ_T
			L.E.	R.E.						
LUT	BR1	6 mo.	70	95	165	160	13	0	73	34
NEP	BR2	4 mo.	104	114	205	190	29	12	82	20
NAP	BR3	4 mo.	62	86	160	205	53	29	78	30
KAI	BR4	18 mo.	52	-60	-10	-5	31	40	67	20
SAM	BR5	7 mo.	85	79	164	152	12	18	87	25
CAR	BR6	$3\frac{1}{2}$ mo.	22	50	59	50	18	30	101	49
MAS	BR7	8 mo.	49	94	160	179	19	25	-	-
PET	N1	6 mo.	-	-	0	3	9	63	66	19
TAB	N2	7 mo.	-	-	0	-2	6	60	68	26

Flaxedil (gallamine triethiodide). Paralysis was maintained throughout the experiment with a constant (i.v.) infusion of 10 mg/Kg/hr Flaxedil and 10% dextrose in normal saline. Artificial hyperventilation was begun immediately after paralysis with a gas ratio of 80% N_2O and 20% O_2 for the craniotomy and a ratio of 75% N_2O to 22.5% O_2 and 2.5% CO_2 throughout the recording session. All areas of incision were covered with 2.5% xylocaine jelly and animals were routinely injected intramuscularly with 200,000 units of a general wide spectrum antibiotic and with 2 mg of dexamethosone at the beginning of each recording session. Initially the crown of the postlateral gyrus above either area 17 was exposed in the normal and BR animals. In MR animals, the cortex contralateral to the rotated eye was exposed. In most cats only one electrode penetration was made, though in two of the group MR cats and in three of the group BR cats, additional penetrations were either made in the second hemispheres or into projection areas of the peripheral visual field. Electrode penetrations were usually made in the region of the area centralis projection and then angled 5-15° anteriorly and medially 5-10° in order to maximize the probability of crossing many ocular dominance columns (Hubel, Wiesel and LeVay, 1976; Shatz, Lindström and Wiesel, 1977). The recording session lasted from 24-30 hr.

The electrocardiograms were monitored continuously. Temperature was maintained at 37°C and expired CO_2 at 3.5-4%.

Optics

The eyes were dilated with 1% Cyclogyl and the nictitating membranes withdrawn with 2.5% Neosynephrine. Contact lens of zero power (6-9 mm radii of curvature) were used to protect the corneas. The size of contact lens was chosen to give the sharpest focus of the image of the optic disc and area centralis of the retina on the tangent screen.

The image of the retina was projected by reflection onto the screen, by means of a variable intensity projector lamp from which light was collected and transmitted to just in front of the eye in a small beam (about 6 mm in diameter) by a fiber optic cable, which caused a broad cone of reflection (about 50° of arc) to be thrown onto the tangent screen (Pettigrew, Cooper and Blasdel, in preparation). Thus the whole tapetal retina was visualized simultaneously. This method gives a very clear image of the area centralis which appears as a greenish patch on the yellow background of the reflection of the tapetum. The retinal landmarks were located easily and the optic disc and area centralis drawn within 10-15 sec, at a light intensity on the retina comparable to that found in an opthalmoscope with a quartz halide lamp (Fernald and Chase, 1971). Prolonged use of such a light source would probably cause substantial bleaching of the retina.

Recording methods and visual stimulation

After the craniotomy a small plastic chamber was cemented to the skull around the open area, and the microelectrode was introduced into the cortex through a small hole in the dura. The cortex was stabilized by pouring agar and a layer of wax into the chamber around the electrode. A custom-built stepping motor micromanipulator was used to advance the electrode up or down in discrete steps of 1 μm or more.

We used tungsten-in-glass microelectrodes (Levick, 1972) with an exposed tungsten tip of 10-15 μm and 2 μm diameter. The signal from the electrode was first fed into a conventional high impedance preamplifier and from there to an oscilloscope for observation of spike waveforms. The response discharges were also played through an audio monitor. Additional circuitry was available for converting the nerve cell spikes into pulses accepted by a minicomputer (NOVA 2) for immediate playback or for storage and later analysis. Preliminary receptive field plots were always done by hand. Cells were assigned an ocular dominance group on the basis of Hubel and Weisel's (1962) seven category classification system. Groups 1 and 7 units are driven only by the contralateral or ipsilateral eye respectively under conditions of monocular testing. Groups 2 and 6 cells are dominated by one eye but are able to be shown to be influenced by the other. Groups 3 and 5 units are still dominated by the contralateral or ipsilateral eye but also have receptive fields for the other eye. Group 4 cells are approximately equally driven by both eyes.

Visual stimuli were presented on a rear projection screen 57 cm from the nodal point of the eye where 1 cm on the screen represents 1^{o} of visual angle at the retina by a custom-built projector which allowed joystick control of position, orientation and size of the light slit. The stimulator was wired into the computer system so that stimuli could be manually and automatically presented. Background illumination was maintained in the mesopic range and the light slit was 1-2 log units brighter. As the electrode was advanced a visual noiseboard was used to activate units which were not firing spontaneously.

Histology and anatomy

A series of microlesions was made by an 8 μA current (negative at the electrode) for 5-10 sec at several depths in each penetration.

At the end of each recording session animals were given an overdose of Nembutal and then perfused through the heart with isotonic saline followed by 10% formalin in saline. A block of the brain was taken from the region of the penetration and then cut into a series of 40 μm sections on a freezing microtome. Sections were stained with cresyl violet. The area of 17/18 border was defined (Otsuka and Hassler, 1962) and the track reconstructed from the electrolytic lesions.

Detailed gross dissections were made of the orbits of the rotated eyes of several of the animals with large angles of rotation, as a means of determining what the pattern of muscle reattachment was.

Eye movements

Observations of the eye movements in our cats were initially made informally and then later several animals with larger angles of rotation had head bolts fitted so that they could be held in the stereotaxic apparatus for more precise observation of the eye movements. These animals were trained to sit quietly in a restraining bag and encouraged to follow with their eyes a visual stimulus on a tangent screen ahead of them. Sequences of eye movements were then filmed with a 16 mm movie camera and later analyzed.

Results

Electrophysiology

Ocular dominance in normal cats

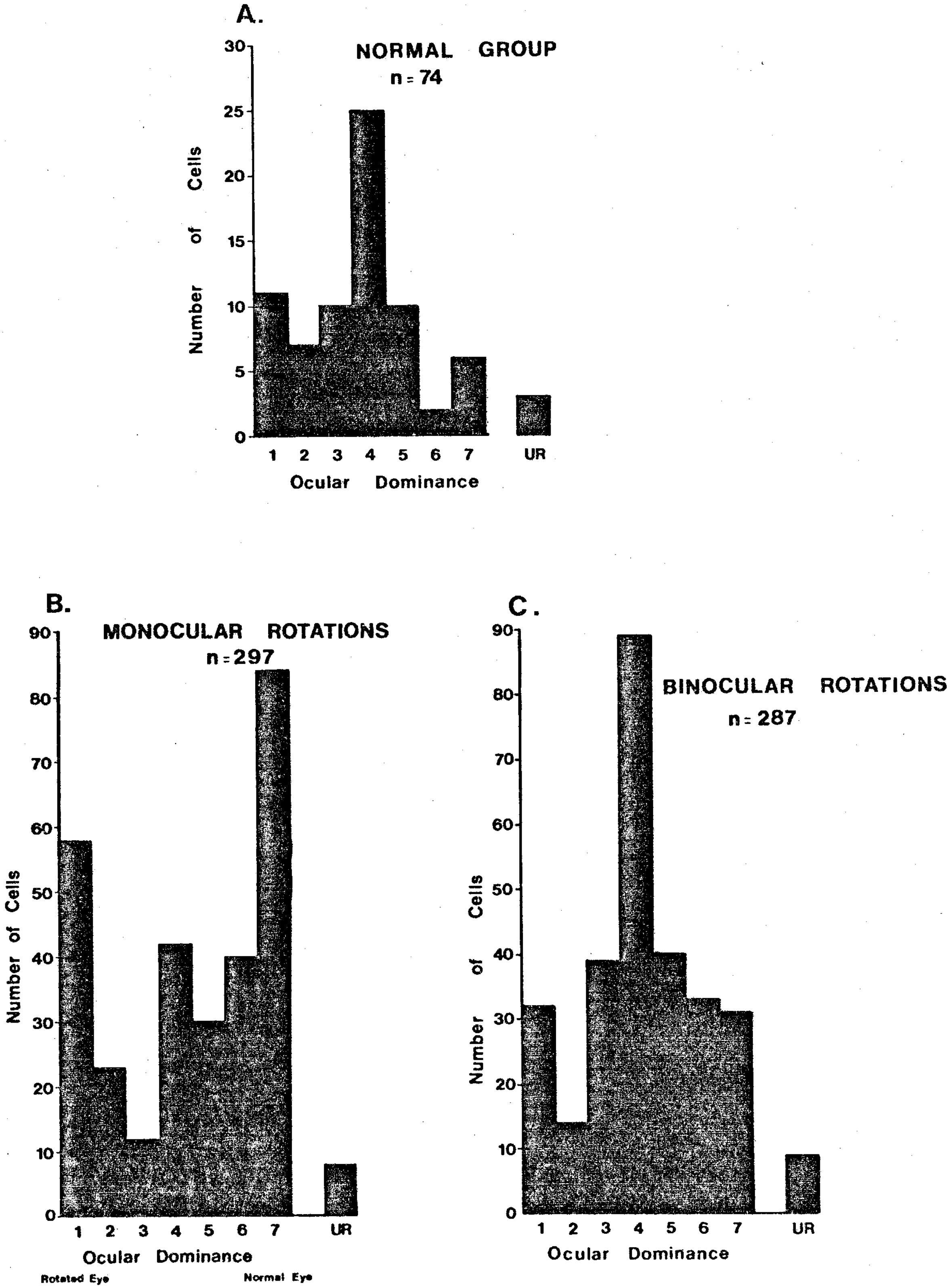
We have recorded from 74 cells in two electrode penetrations in area 17 of two normal animals in order to confirm that our procedures and preparations were substantially similar to those previously reported. The combined ocular dominance distribution is shown in Fig. 2A. 54 or 73% of the cells were binocularly driven (groups 2-6). The comparatively large number of monocular units were recorded from N2 where the penetration sampled extensively from receptive fields within 2° of the area centralis. The average length of the penetrations was 2.73 mm.

Fig. 2. Ocular dominance (O.D.) histograms for the three groups of animals shown in terms of the seven point classification system of Hubel and Wiesel (1962), where cells driven exclusively by the eye contralateral to the recording electrode are put in group I and those driven only by the ipsilateral eye are put in group 7.

A. The ocular dominance distribution for the two normal cats (group N). The number of cells sampled was 74, of which 73% were binocular, that is in O.D. groups 2-6.

B. The combined ocular dominance distribution for the eleven animals given monocular rotations varying from 3^o-200^o at the time of natural eye opening (group MR). The cells driven exclusively by the rotated eye are shown in group 1 and those driven exclusively by the normal eye are shown in group 7. The total number of cells sampled was 297 of which 49% were binocular. This is a comparable, though slightly higher percentage than the figures reported by Blakemore et al. (1975) and Yinon (1975). However as our kittens were younger than those of Blakemore et al. (1975) and only 35% of the cells recorded had receptive fields within 5^o of the area centralis the difference is probably insignificant.

C. The combined ocular dominance distribution for the eight animals given binocular rotations (group BR) at the same age as the kittens in group MR. 287 cells were recorded, of which 75% of the units were driven by both eyes. These cells were truly binocular with 56% of the sample having well-defined receptive fields (i.e., O.D. groups 3, 4, and 5) for both eyes. Furthermore as 52% of cells had receptive fields within 5^o of the area centralis the high degree of binocularity is even more surprising.


A.
NORMAL GROUP
n = 74
30
25
20
15
10
5
0
Number of Cells
1 2 3 4 5 6 7 UR
Ocular Dominance
B.
MONOCULAR ROTATIONS
n = 297
90
80
70
60
50
40
30
20
10
0
Number of Cells
1 2 3 4 5 6 7 UR
Ocular Dominance
Rotated Eye
Normal Eye
C.
BINOCULAR ROTATIONS
n = 287
90
80
70
60
50
40
30
20
10
0
Number of Cells
1 2 3 4 5 6 7 UR
Ocular Dominance

46% of the units recorded lay within 5° of the area centralis, 49% between 5° and 10° and only 5% further into the periphery. The receptive field properties have been analyzed and then summarized in Tables I and II.

Ocular dominance in cats reared with a monocular rotation

Cortical cells have been recorded in 11 penetrations through area 17 of 10 cats. The combined ocular dominance histogram (Fig. 2B) for these animals has been prepared after recording contralaterally to the rotated eye and ipsilaterally to the normal eye for all but one animal where penetrations were made in both hemispheres. Here the ocular dominance of cells from the second penetration have been reported in terms of number driven by the rotated eye (group 1) or by the normal eye (group 7). Two of these animals, MR1 and MR10 with a 10° and 200° monocular intorsion respectively, were raised with suture of the normal eye from 5 and 3 weeks until 14 weeks. In both animals the majority of cortical cells eventually came to be driven by the open rotated eye.

Of the 263 cells recorded from the other 8 animals 39 (16%) were driven by the rotated eye alone, 75 (29%) were driven by the normal eye, and 143 (54%) were binocular. However, of these binocular units only 80 or 30% had good receptive fields in both eyes. Our percentage of binocular units is slightly higher than that reported by Blakemore *et al.* (1975) and Yinon (1975). However, all our animals were younger and totally inexperienced at eye rotation whereas at least 3 of Blakemore *et al.*'s kittens had 1-2 weeks visual experience. Secondly only 31% of the cells sampled lay within 5° of the area centralis which should increase the probability of finding binocular units (Albus, 1975). Thirdly a week's immobilization may have little effect on the cortex at a young age.

The results from individual animals did not show great variation although there was a slightly higher percentage of binocular units in the animals who were raised without any forced usage of the rotated eye throughout the critical period. An ocular dominance histogram for one of the animals which had been trained for the behavioral experiment, AAG (MR9), (Table I, Chapter II), is shown in Fig. 3. AAG showed very good visuomotor ability with the rotated eye and fairly high levels of interocular transfer between the rotated and normal eye despite the low percentage of cells in area 17 dominated by the rotated eye. There was no correlation between angle of rotation and percentage of binocular units.

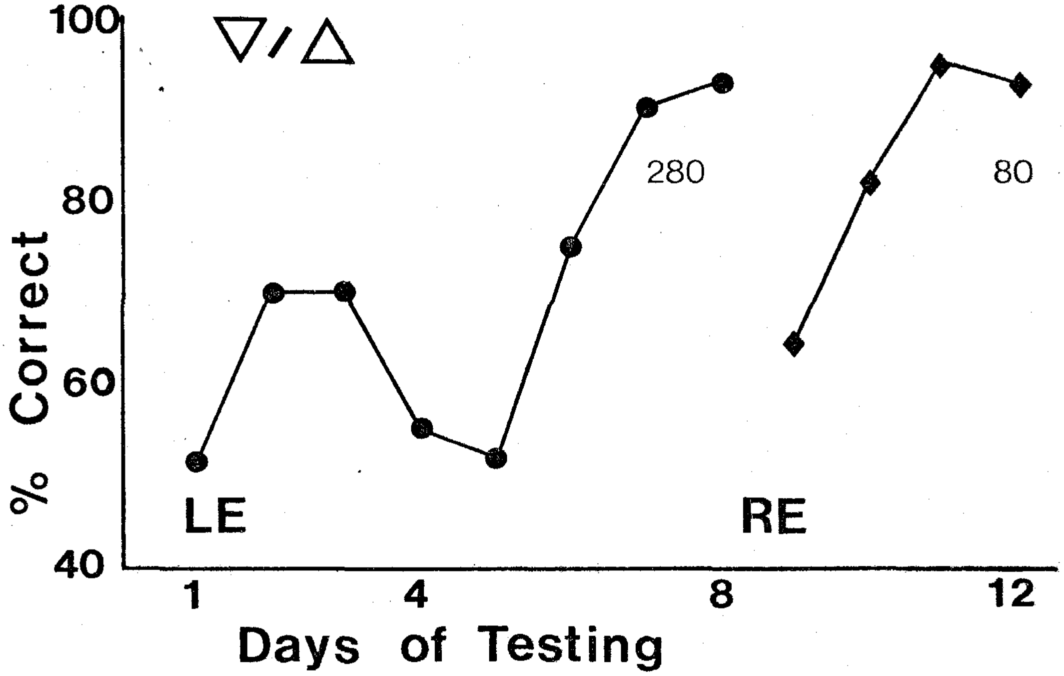
Most of the receptive fields of cells recorded lay within 10^{o} of the area centralis; 30% in group MR and only 5% in group N were further than 10^{o} into the periphery. In all cases cells retained their normal retinotopic relationship to each other and to the retinal landmarks. Receptive field sizes did not differ significantly between the two groups.

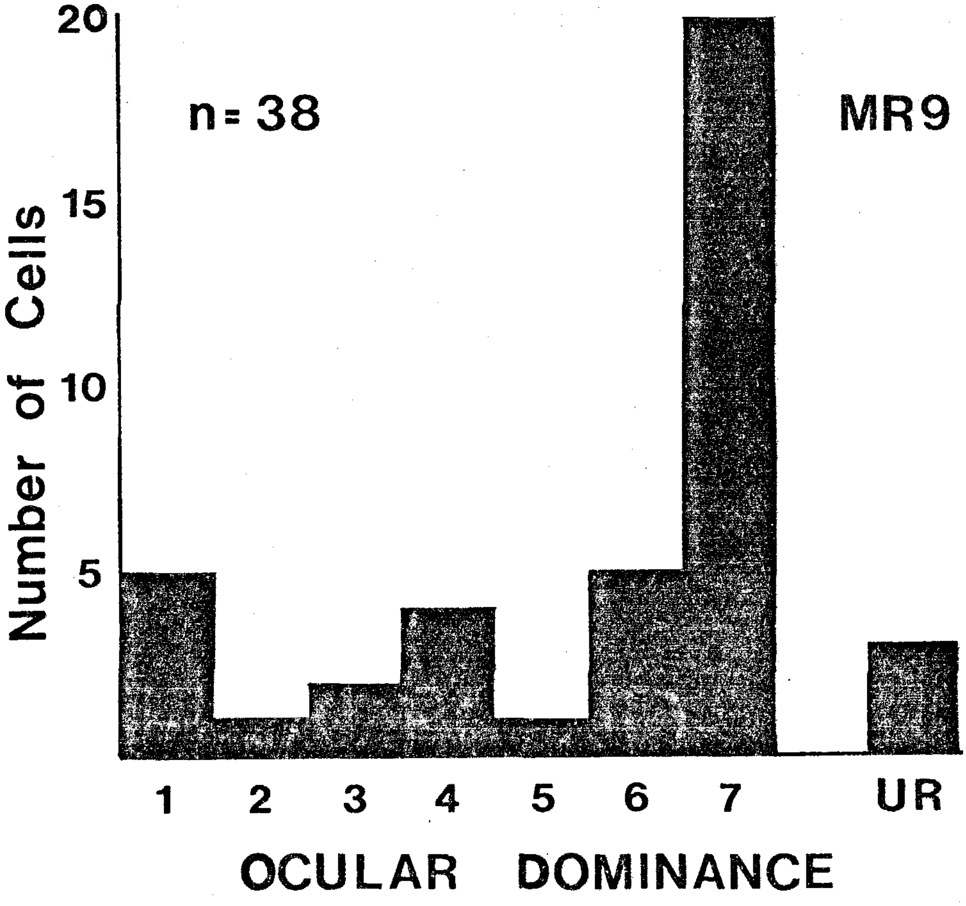
Ocular dominance in cats reared with binocular rotations

In view of the comparatively low degree of binocularity of the animals with monocular rotations we were surprised to find that 215 out of the 287 cells (75%) recorded in 11 area 17 penetrations of the eight group BR animals, were binocularly responsive. The combined O.D. histograms for these penetrations are shown in Fig. 2C.

Although the high binocularity was unexpected in the first animal, BR1, the next 7 animals showed very similar ocular dominance distributions despite the presence of considerable divergent squints in addition to the rotational displacements in all animals. Most of the cells were truly binocular and not just marginally influenced by the second eye; for 161 or 56% of the units recorded,

Fig. 3. Ocular dominance histogram for one of the animals in the MR group which was given a monocular rotation of 45° at 8 days of age. Animal MR9 (AAG) was previously trained for the behavioral experiment described in Chapter II. The learning curve for this animal's performance on the most difficult orientation discrimination problem is shown above the ocular dominance histogram drawn after recording in the cortex contralateral to the animal's left rotated eye. This animal showed considerable interocular transfer of several of the two-choice orientation discriminations despite the very low percentage of binocular neurons seen (31%) indicating that interocular transfer of discrimination learning is largely independent of area 17 binocularity.


▽/△
100
80
60
40
% Correct
280
80
LE
RE
1
4
8
12
Days of Testing


20
15
10
5
Number of Cells
n= 38
MR9
1
2
3
4
5
6
7
UR
OCULAR DOMINANCE

receptive fields could be drawn through both eyes. These cells were categorized in ocular dominance groups 3, 4, and 5.

The angular distances between the area centralis of individual cats varied from 10^{o} to 64^{o}. The average length of the penetrations in the group BR animals was 2.22 mm. In three cats we recorded from both hemispheres, but the ocular dominance distributions did not differ significantly between the two sides of the brain. The results for individual animals did not differ greatly from the combined results, as can be seen from Fig. 4A and 4B. Fig. 4A shows the ocular dominance histogram for the animal BR5 with the greatest area centralis separation, 64^{o}, and Fig. 4B shows the distribution for the cat BR4 with one eye intorted and one eye extorted.

Although receptive fields were recorded as far as 20^{o} from the area centralis, 82% came from within 0^{o} of the area centralis (52% lay within 5^{o}; 30% lay between 5^{o} and 10^{o}) in group BR and 75% in group N. Thus, our three samples are fairly comparable in terms of position within the visual field (cf. Albus, 1975). The only cortical laminar in which reduced binocularity was observed in group BR was layer IV where many of the simple cells (Hubel and Wiesel, 1962) were monocular. This has also been confirmed histologically.

Receptive field sizes

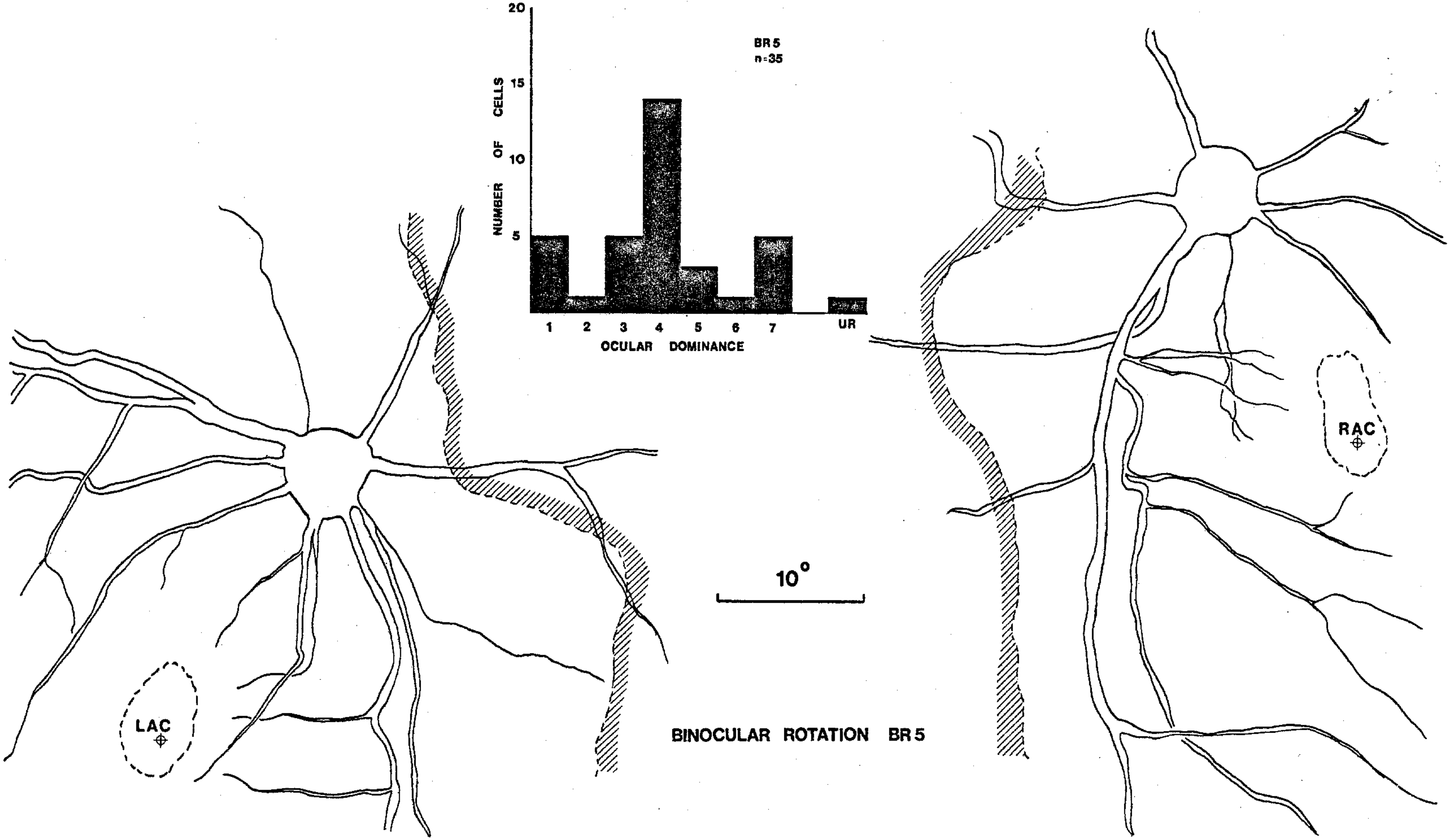
Despite the wide divergence of the visual axes of the two eyes of most of the animals in group BR, the receptive fields recorded showed normal retinotopic position with respect to each other and the retinal landmarks. In general the receptive fields of the MR and BR animals are slightly larger than those for the normals at the same eccentricity. The average mean core size of the receptive fields (Pettigrew, Nikara and Bishop, 1968) was 2.1^{o} for group BR, whereas that

Fig. 4. Ocular dominance distributions for two of the animals with binocular rotations.

A. shows a fiber optic projection of the retinal landmarks for animal BR5 which had two 90° intorsions and whose areae centrales were separated by the largest angle (64°) as measured on the tangent screen. The relative positions of the landmarks for the two eyes have not been changed to allow superimposition of the ocular dominance histogram. The hatched lines represent the edges of the tapetum for the two eyes. LAC and RAC indicate the left and right area centralis respectively. The dotted lines indicate the horizontal streak which appears as an area of more intense green on the yellow background of the tapetum when using the fiber optic reflection technique. Even in the case of this animal with this large distance between the areae centrales of the two eyes the percentage of binocular units sampled was 70%.

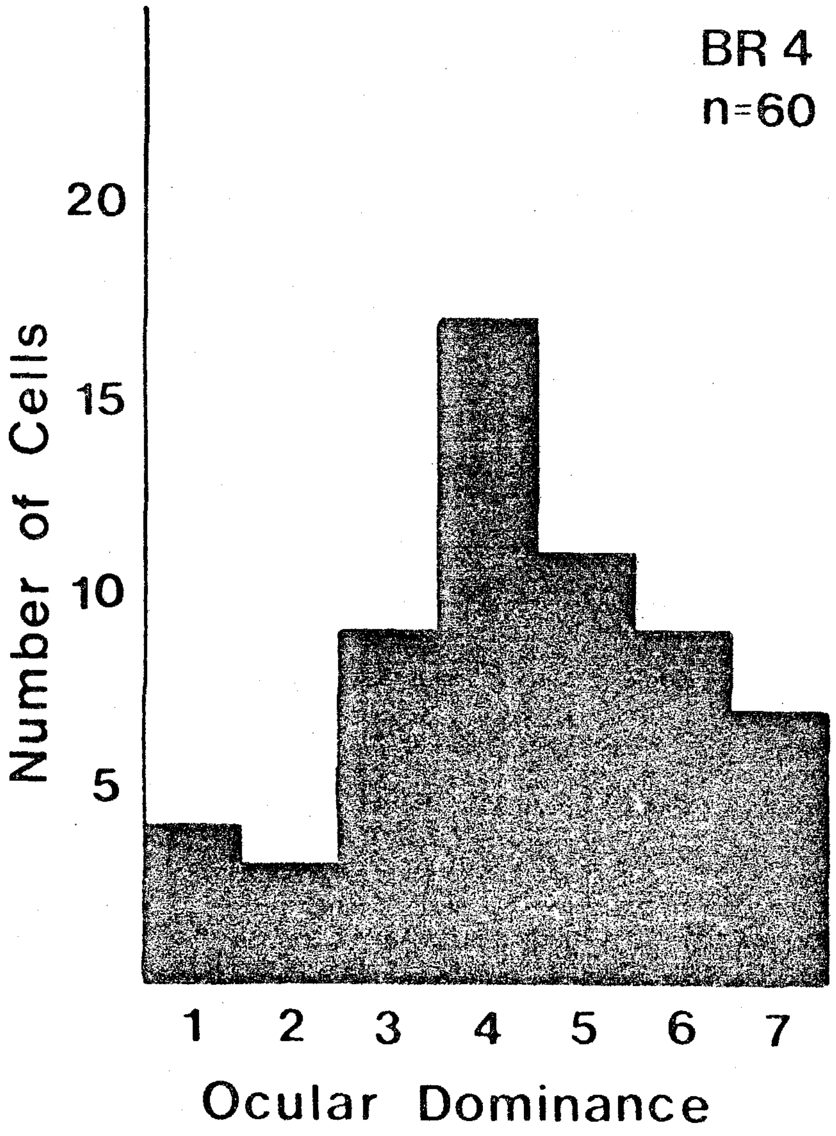
B. shows the ocular dominance histogram drawn for cat BR4 whose eyes were rotated in parallel. The left eye was extorted 50° and the right eye intorted by 60°. The vertical disparity was 45°. The cortex of this animal also showed a normal ocular dominance distribution.

A.



BINOCULAR ROTATION BR5

B.



for the normal group was 1.8°. This difference is significant ($p = 0.025$ for a 2-tail test). However, as the cells sampled from the BR animals are more difficult to drive than those from normal animals systematic errors may account for the difference.

Orientation selectivity

In groups MR and BR the orientation tuning ranges of the receptive fields drawn through the rotated eye (or eyes) were broader than those for the receptive fields mapped through the normal eye, or for the fields drawn through either eye of the normal animals. Scatter plots of the width of orientation tuning for the receptive fields drawn through each eye of binocular units in ocular dominance groups 3, 4, and 5 are shown for the three groups of animals in Figs. 5A, B, and C. The mean of the orientation tuning width for these cells for the group MR animals was 81° for the rotated eye and 77° for the normal eye, 82° for the group BR animals, and 67° for the normal animals (see Tables I and II). Tuning width has been defined as the range of orientations over which a stationary bar of optimal length will elicit a response from a particular cortical neuron (Pettigrew, Nikara and Bishop, 1968).

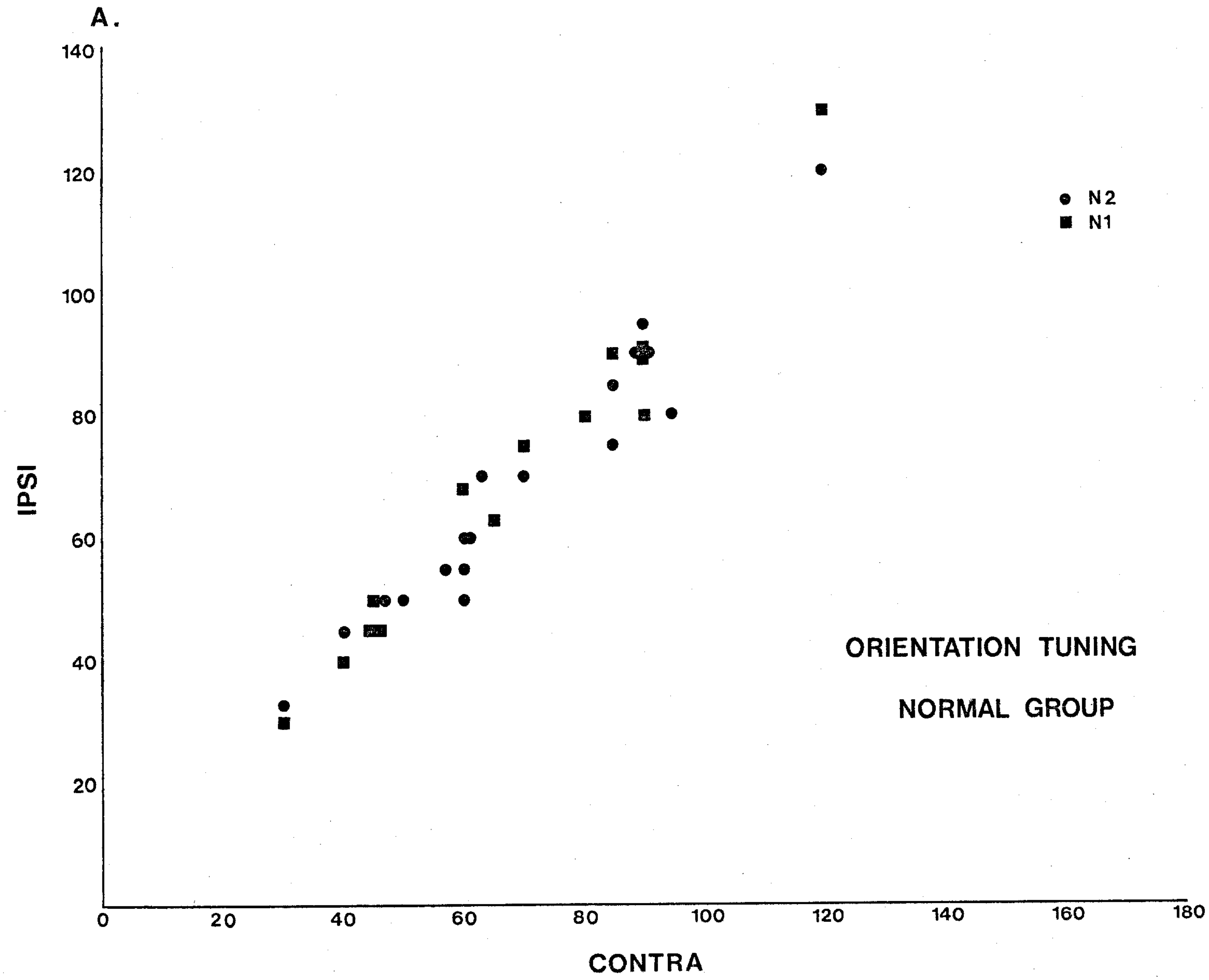
The angular disparities between preferred orientations of the receptive fields mapped through both eyes of binocular neurons from O.D. categories 3, 4, and 5 were much larger in groups MR and BR than in group N. Scatter plots of the preferred orientations of the binocular units in group N, MR, and BR respectively are shown in Figs. 6A, B, and C. In the case of group MR animals the angle of rotation after paralysis has been subtracted from the preferred orientation of the rotated eye. In the case of group BR animals the angle of rotation for each eye after paralysis has been subtracted from the angle of preferred orientation

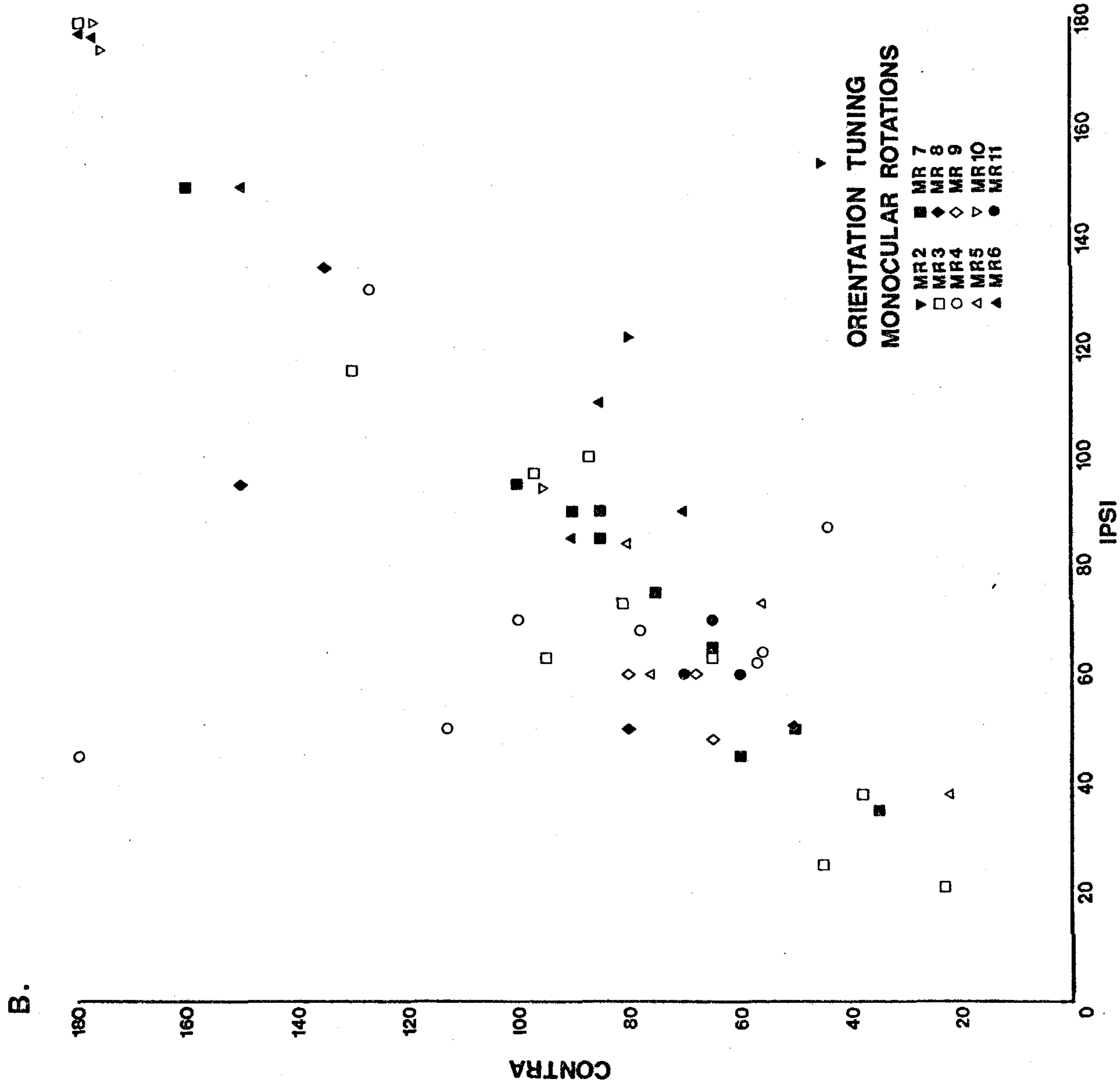
Fig. 5. Scatter plots of the orientation tuning of the receptive fields drawn through the two eyes for binocular neurons in ocular dominance groups 3, 4, and 5 in the three groups of animals. Orientation tuning width is the range of orientations over which a stationary bar will elicit a response from a particular cortical neuron.

A. Orientation tuning for the normal group. The mean orientation tuning width for this group is 67^{o}.

B. The orientation tuning scatter plot for the group of animals with monocular rotations shows a greater standard deviation from the regression line than does the normal group. The mean tuning width for the receptive field drawn through the normal eye of these animals was 77^{o}, and the mean for the receptive field drawn through the rotated eye was 81^{o}.

C. The orientation tuning scatter plot for the first seven animals in the group BR. The standard deviation of the orientation tuning widths for binocular cells sampled from these animals with bilateral rotation is greater than that for either the normal or the MR group. The mean for this group is 87^{o}.


A.
ORIENTATION TUNING
NORMAL GROUP
● N2
■ N1
IPSI
140
120
100
80
60
40
20
CONTRA
0
20
40
60
80
100
120
140
160
180


B.
ORIENTATION TUNING
MONOCULAR ROTATIONS
▼ MR2
☐ MR3
○ MR4
△ MR5
▲ MR6
■ MR 7
◆ MR 8
◇ MR 9
▽ MR10
● MR11
CONTRA
180
160
140
120
100
80
60
40
20
0
IPSI
0
20
40
60
80
100
120
140
160
180

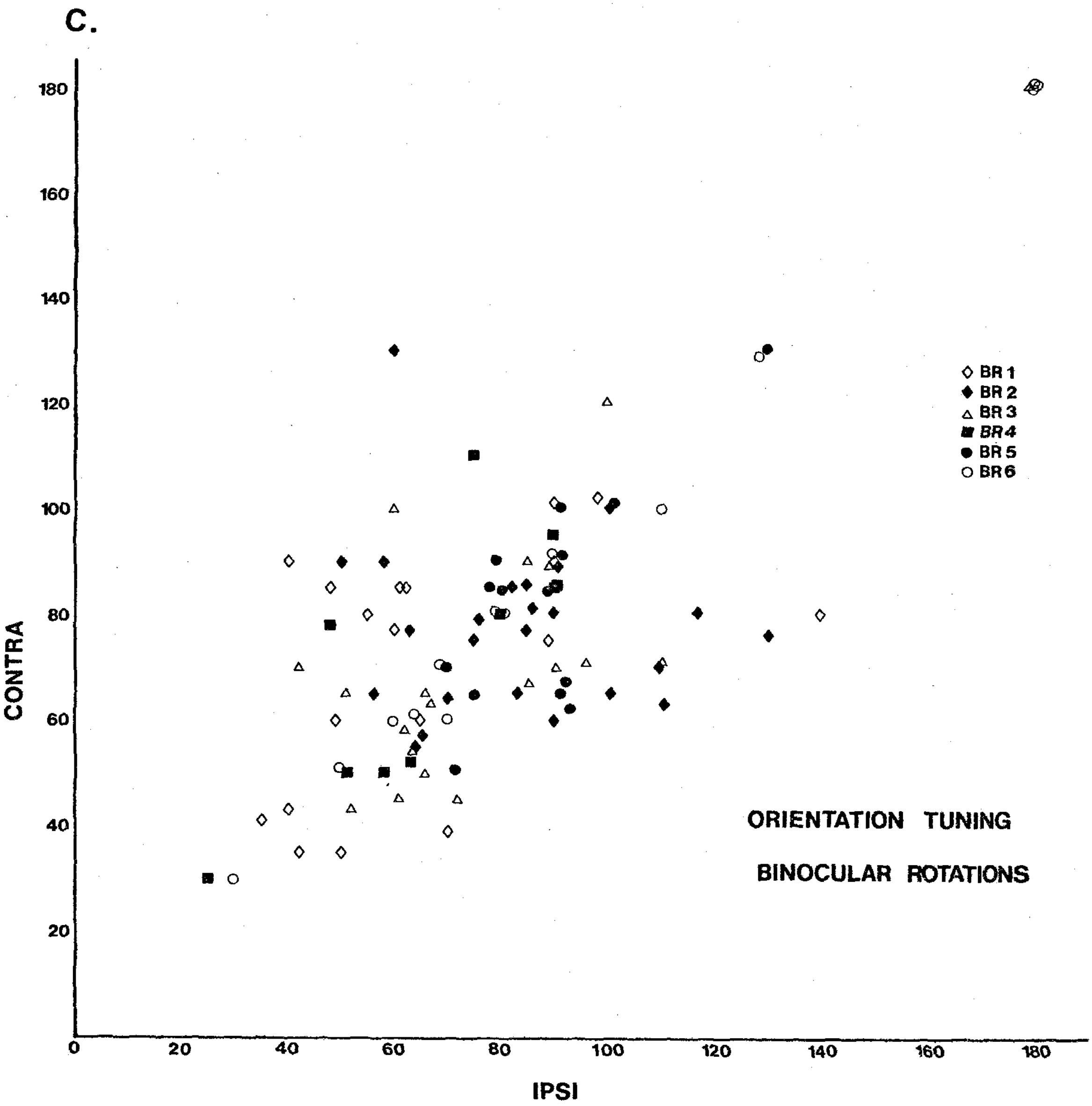
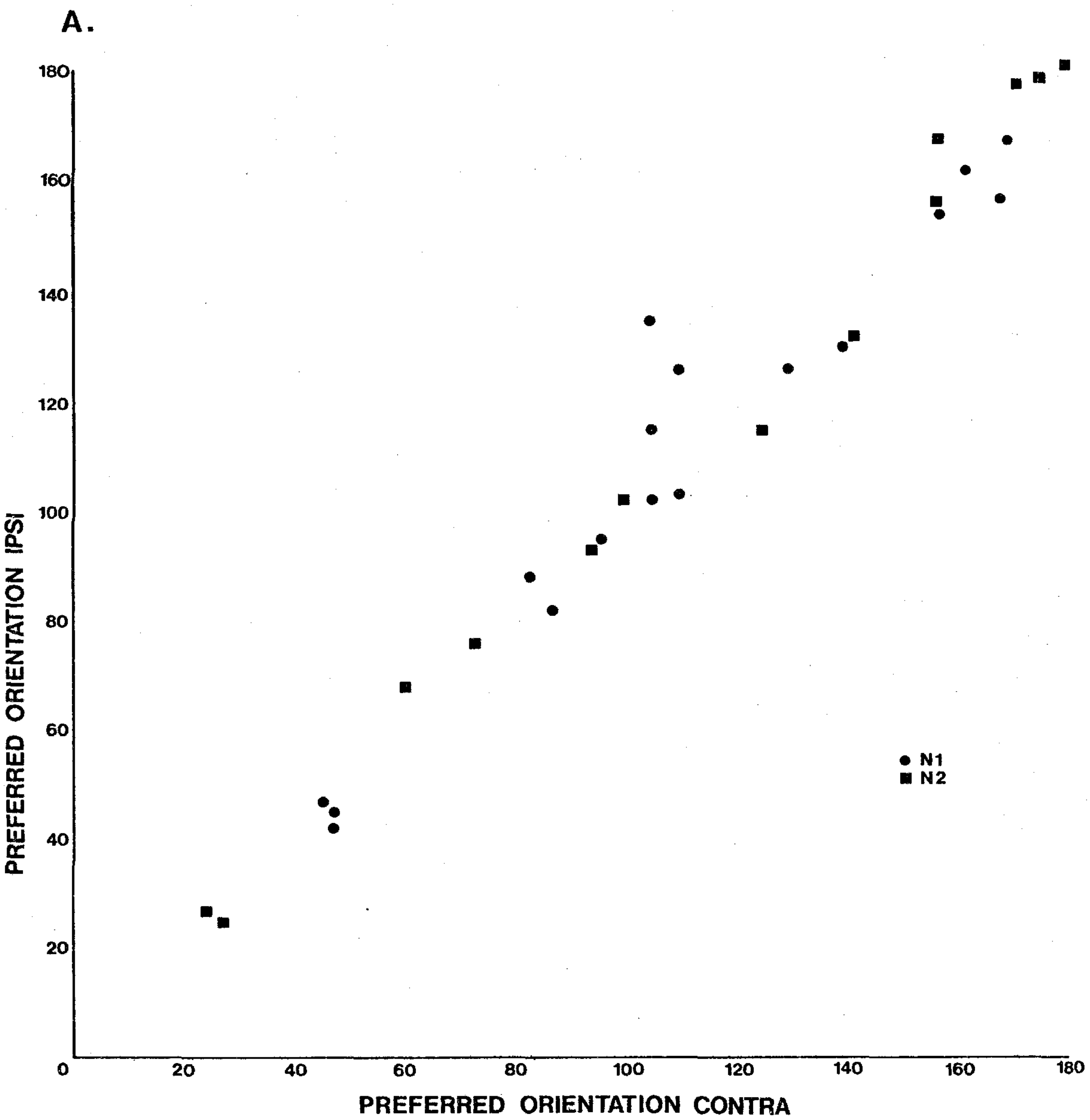

C.
CONTRA
IPSI
0
20
40
60
80
100
120
140
160
180
◇ BR 1
◆ BR 2
△ BR 3
■ BR4
● BR 5
○ BR 6
ORIENTATION TUNING
BINOCULAR ROTATIONS

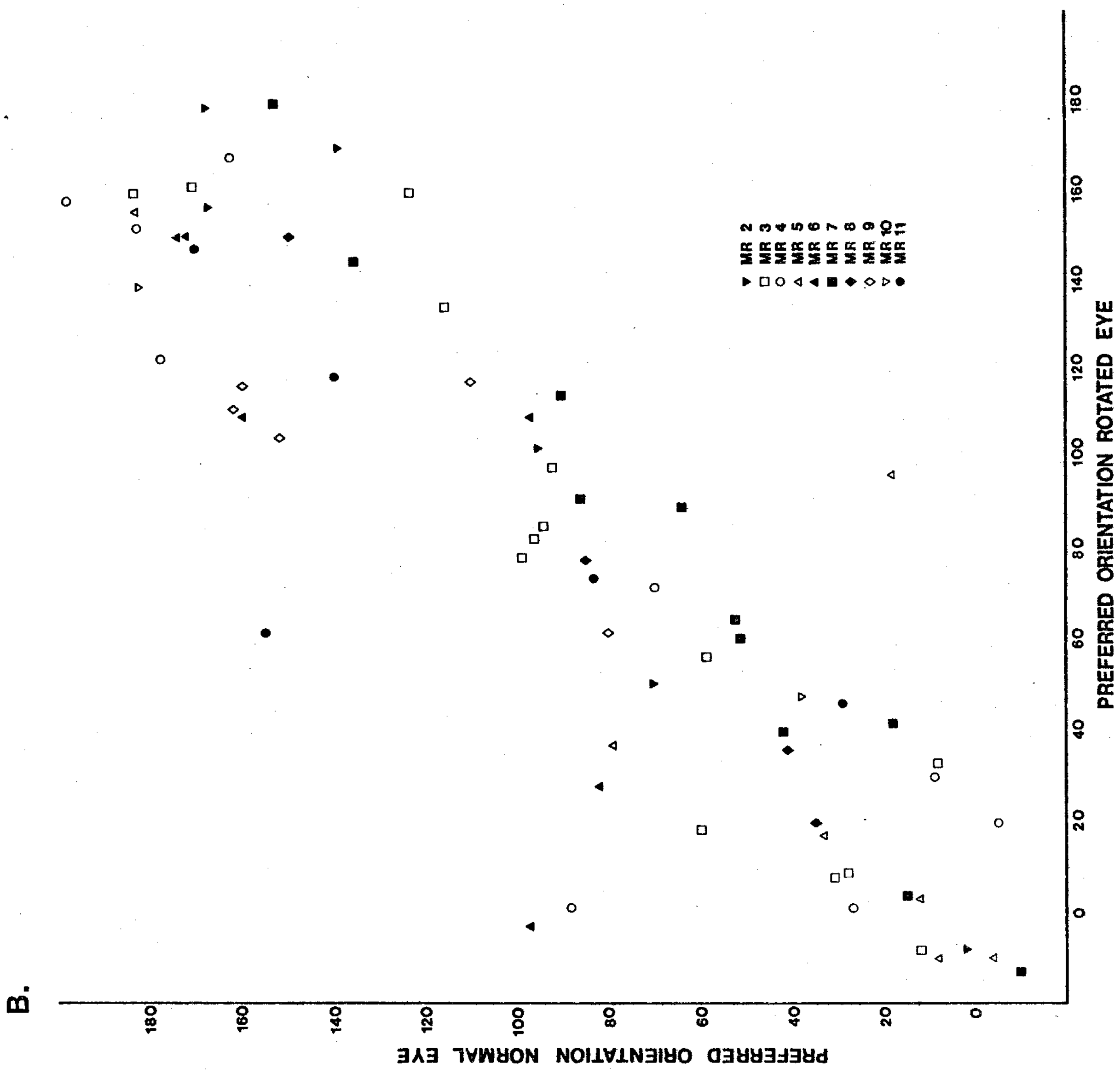
Fig. 6. Scatter plots of the normalized interocular orientation disparities of binocular neurons in ocular dominance groups 3, 4, and 5 for the three groups of animals.

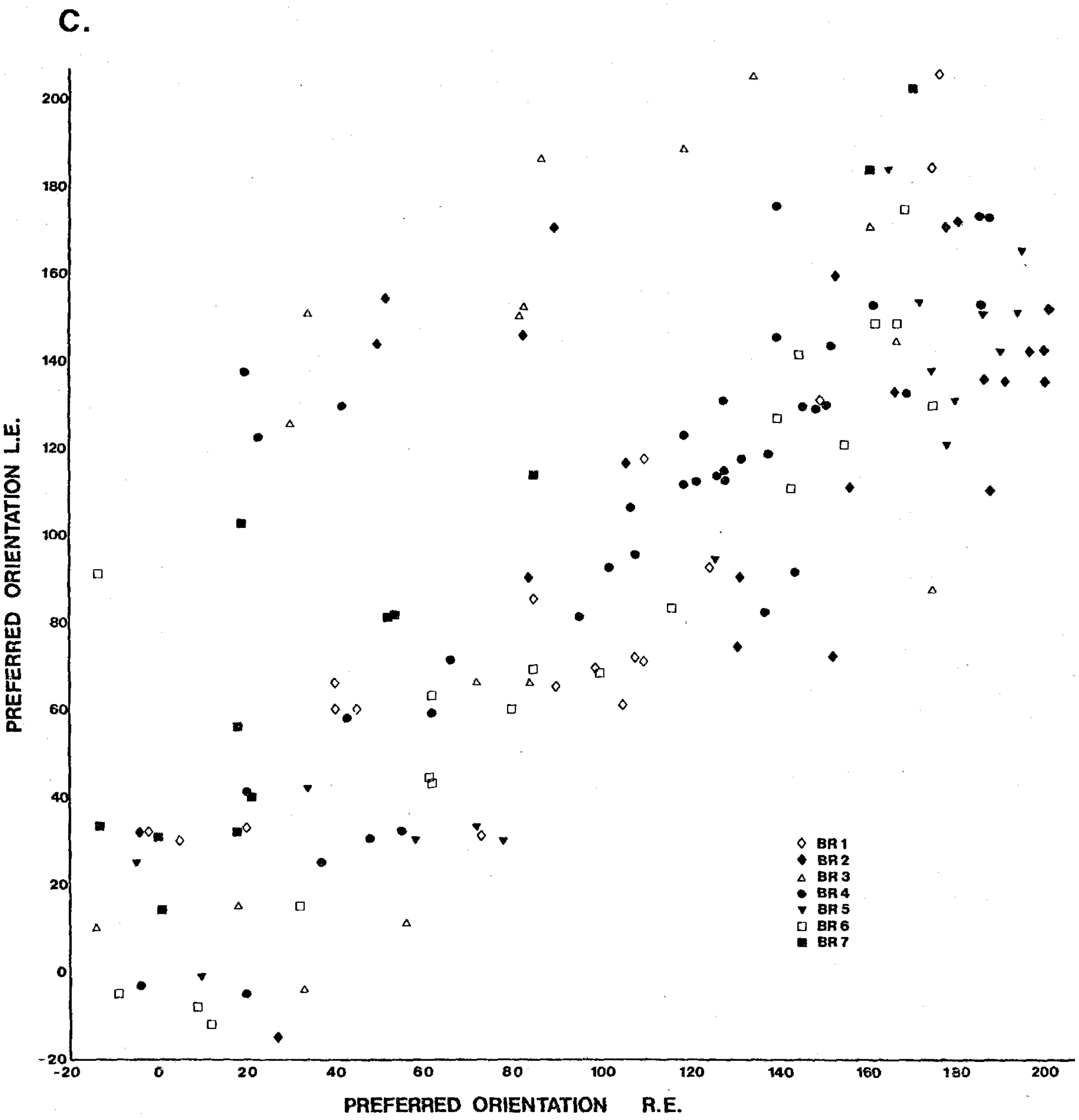
A. Scatter plot of the interocular orientation disparity for the normal group.

B. Scatter plot of the interocular orientation disparities of the binocular units in the MR group. The preferred orientation of the receptive field drawn through the normal eye is plotted against the preferred orientation of the field drawn through the rotated eye after the angle of rotation under flaxedil paralysis has been subtracted.

C. Scatter plot of the normalized interocular orientation disparities of the binocular unit sampled from the first seven BR animals. The preferred orientation of the receptive field drawn through the left eye is plotted against the preferred orientation of the field drawn through the right eye after the total angle of rotation under paralysis has been subtracted out. These data are summarized in Figs. 7A and B.


A.
PREFERRED ORIENTATION IPSI
PREFERRED ORIENTATION CONTRA
0
20
40
60
80
100
120
140
160
180
● N1
■ N2


B.
PREFERRED ORIENTATION NORMAL EYE
PREFERRED ORIENTATION ROTATED EYE
0
20
40
60
80
100
120
140
160
180
▼ MR 2
□ MR 3
○ MR 4
△ MR 5
▲ MR 6
■ MR 7
◆ MR 8
◇ MR 9
▽ MR 10
● MR 11


C.
PREFERRED ORIENTATION L.E.
PREFERRED ORIENTATION R.E.
200
180
160
140
120
100
80
60
40
20
0
-20
-20
0
20
40
60
80
100
120
140
160
180
200
◇ BR 1
◆ BR 2
△ BR 3
● BR 4
▼ BR 5
□ BR 6
■ BR 7

for that eye in order that the results for individual animals could be compared. In similar manner the combined histograms of orientation disparities for all of the neurons of O.D. categories 3, 4, and 5 from all 3 groups have been compiled and are shown in Figs. 7A and B. On the average, the preferred orientations of the binocular cortical cells differed by an amount equal to the combined rotations imposed on the two eyes. Thus, in these coordinates, orientation differences close to 0^{o} were most commonly encountered. However, the standard deviation of the orientation disparity histograms were much larger for the experimental groups than for the group N cats (31^{o} for the MR group, 35^{o} for the BR group compared to 8^{o}) (Fig. 7). Only one cell was found which showed a high correlation between the optimal orientations and directions for the two eyes. This simple cell was seen in BR8 where the combined angle of rotation was approximately 90^{o}. The receptive field positions and orientation response curves for the two eyes are shown in Fig. 8A. Again the orientation tuning was broader for the eye with the larger rotation than for the eye with the smaller rotation. We did not find any other cells in which the preferred orientations showed adjustment to the rotations. However, as the combined angle of rotation between the two eyes for most of the group BR cats was often around 180^{o}, and very few of the binocular cells seen in recording from group MR were orientation selective, such trends would be hard to see.

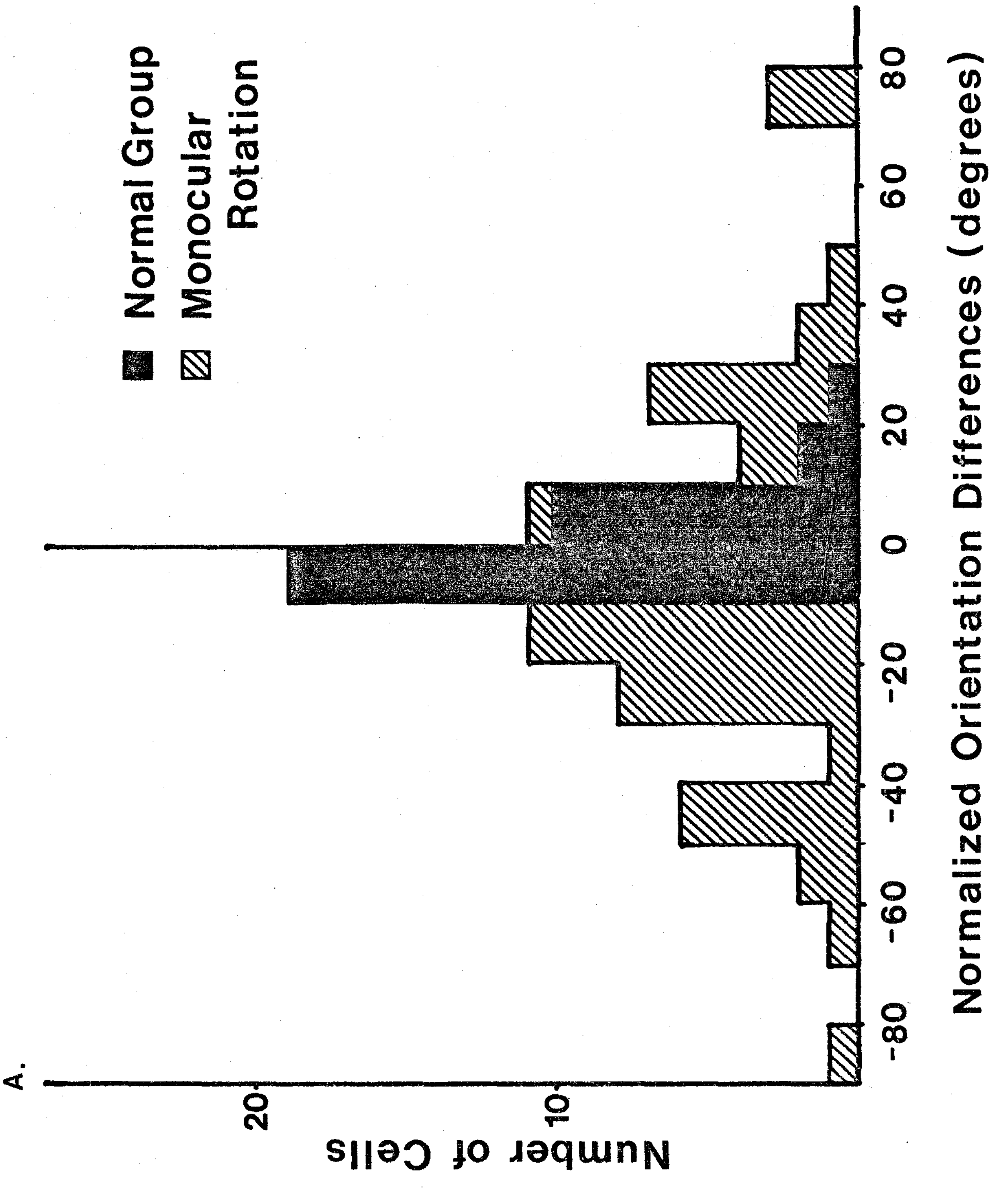
Direction selectivity

Most of the evidence found in area 17 for physiological adaptation to rearing with rotation of the visual world was seen in layer V cells. Several of the units with the properties described by Palmer and Rosenquist (1974) for corticotectal cells, recorded in animals with monocular rotations of 45-135^{o} and in BR8

Fig. 7. Histograms of the normalized interocular orientation disparities for the three groups of animals.

A. Histogram of the normalized interocular orientation disparities for the normal animals and those with monocular rotations. The normalization was done by subtracting the total angle of rotation under flaxedil paralysis from the preferred orientation of the field drawn through the rotated eye. The standard deviations of the two histograms are 8° for the normal group and 31° for the MR group. The mean orientation disparities for the two groups lie close to 0°.

B. Histogram of the normalized interocular orientation disparities for the normal and the BR animals. The normalization was done by subtracting the total angle of rotation from the difference in preferred orientations for the receptive fields drawn through the two eyes. Despite the large divergences of the visual areas and spread of the histogram, the mean and median value for normalized interocular orientation disparities lies close to 0° for the BR group. The standard deviations of the two histograms are 8° for the normal group and 35° for the BR group.


A.
■ Normal Group
▨ Monocular Rotation
Number of Cells
20
10
-80
-60
-40
-20
0
20
40
60
80
Normalized Orientation Differences (degrees)

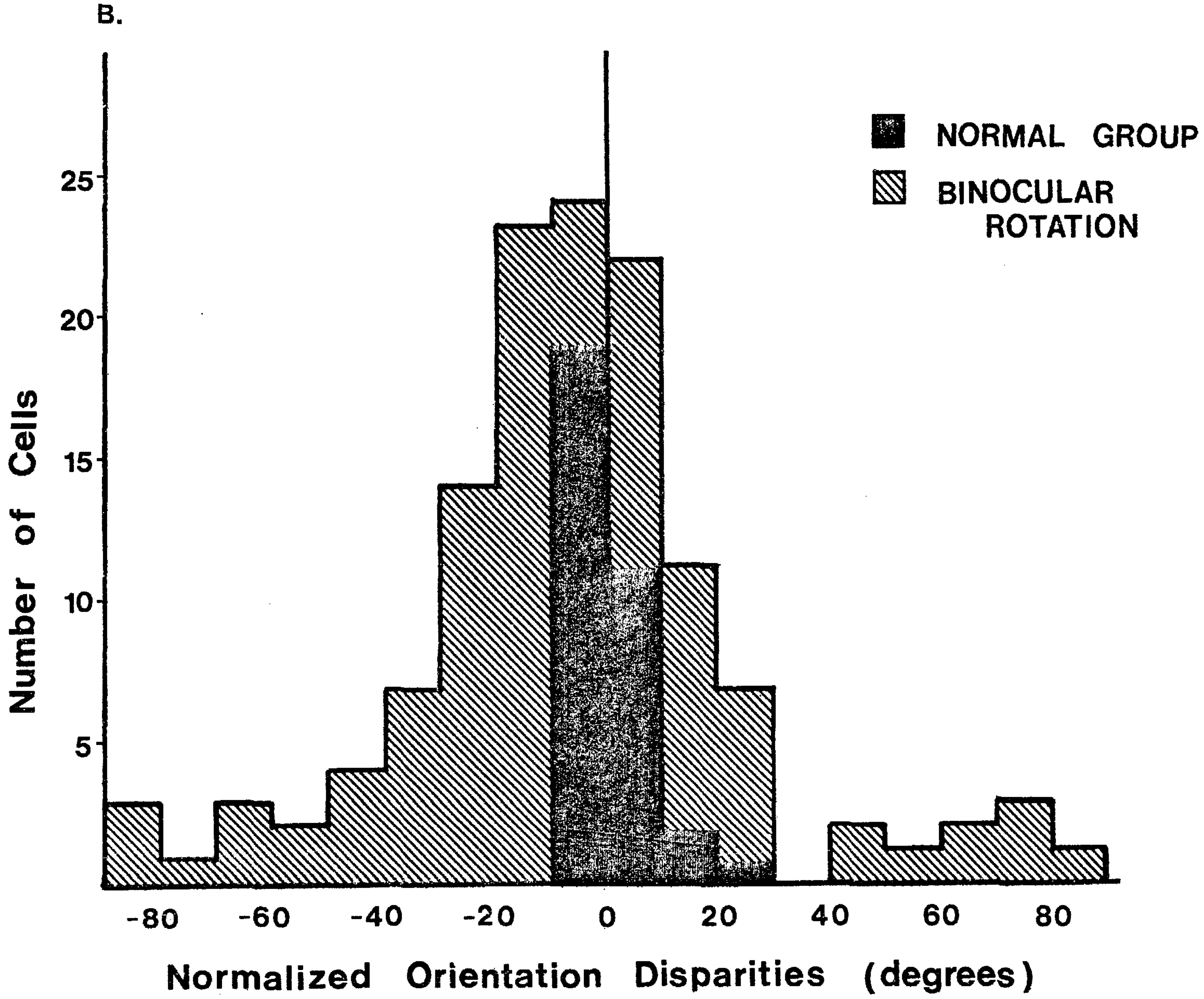

B.
NORMAL GROUP
BINOCULAR ROTATION
Number of Cells
25
20
15
10
5
-80
-60
-40
-20
0
20
40
60
80
Normalized Orientation Disparities (degrees)

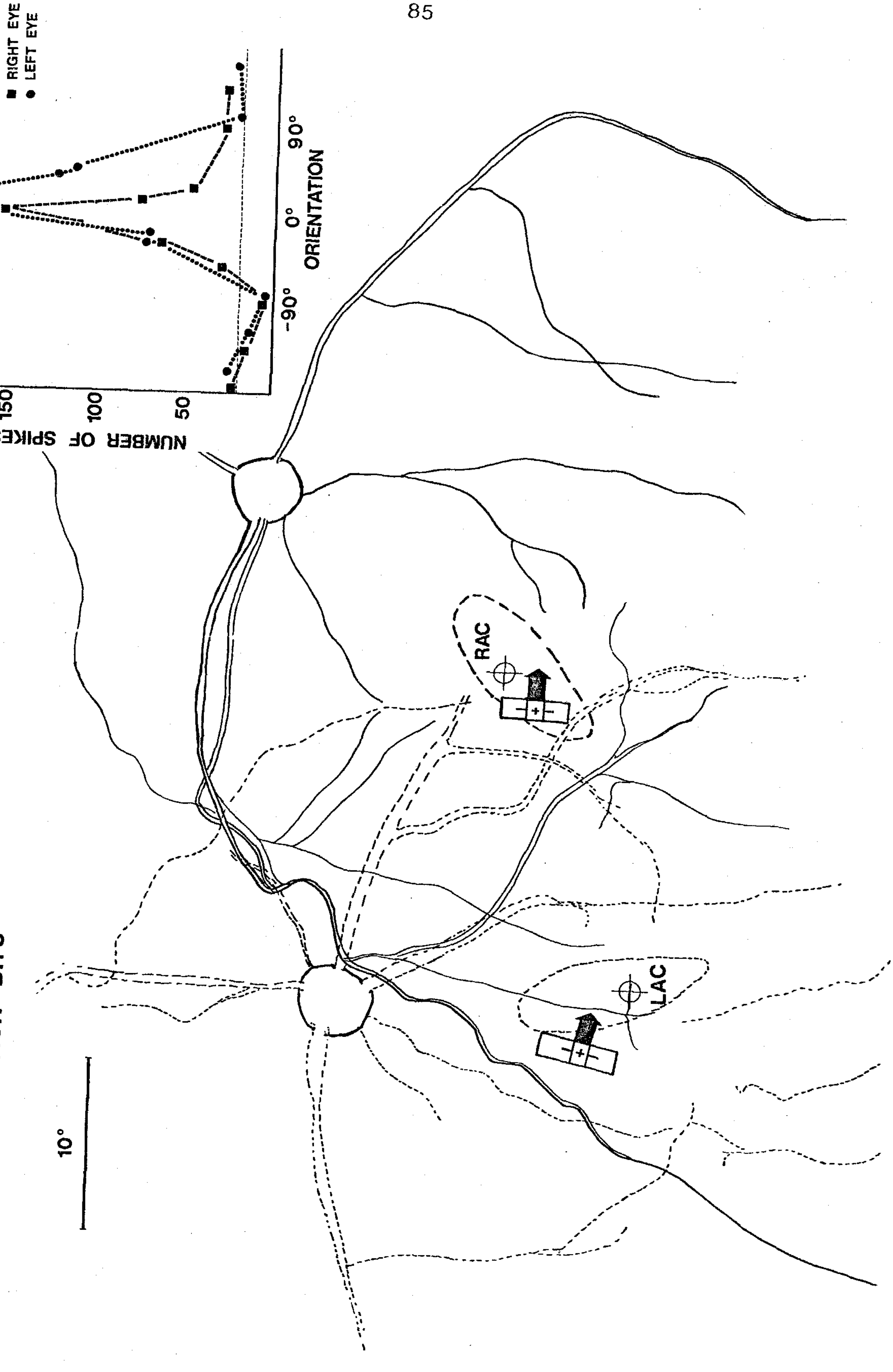
Fig. 8. Receptive field drawings and direction tuning graphs of cells which showed significant shifts in direction selectively, from both the MR and BR groups of animals.

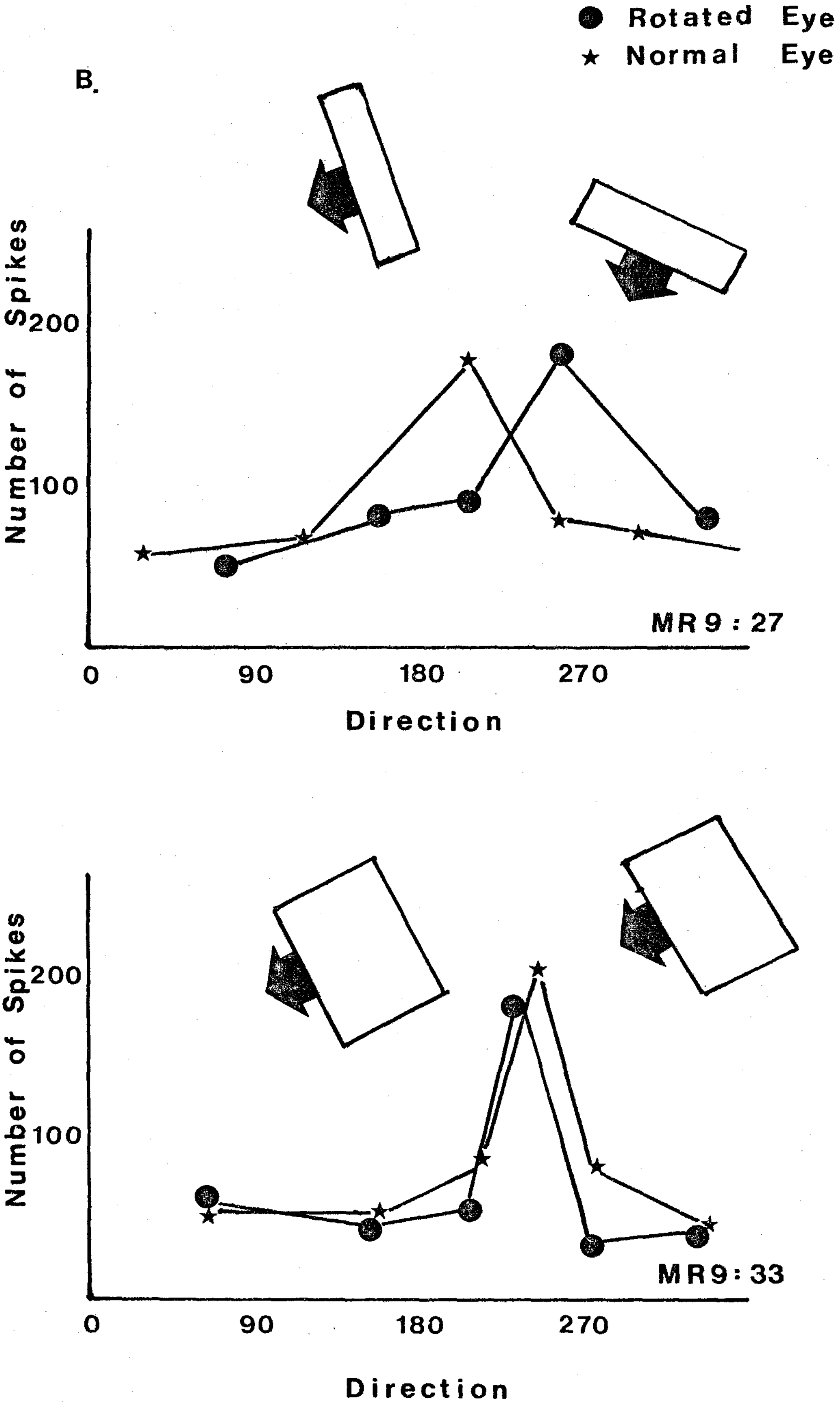
A. shows a fiber optic projection of the retinal landmarks of animal BR8 which had its left eye intorted by approximately 70° and its right eye intorted by approximately 20° giving it a total angle of rotation of 90°.

The only cell in our total sample of approximately 600 units from both experimental groups which showed any change in orientation selectively was the simple, unimodal, direction selective, cell (SUDS cell), whose receptive fields are shown on the diagram. The orientation tuning graphs for the fields drawn through the two eyes are shown in the top left hand corner of the figure.

B. shows the receptive fields of two cells recorded from the same cat, MR9, which had a single rotation of 45°. The first cell (unit 27) shows the normal relation of preferred directions of movement of the receptive fields for most binocular neurons in this animal. The second cell (unit 33) shows the shift in direction selectivity which was observed in several of the cells which had properties comparable to those described by Palmer and Rosenquist (1974) for corticotectal cells.

A. BINOCULAR ROTATION BR 8




● Rotated Eye
★ Normal Eye
B.
Number of Spikes
200
100
MR 9 : 27
0
90
180
270
Direction
Number of Spikes
200
100
MR9:33
0
90
180
270
Direction

showed a significant shift in direction selectivity. Of the 16 corticotectal cells recorded in the MR animals only 10 were binocularly driven, and of these only 5 could be shown to have changed their direction preference to correspond with that of the normal eye. Three others had become omnidirectional and nonselective for direction. One of the cells which changed its preferred direction is shown in Fig. 8B. The four Rosenquist and Palmer layer V corticotectal cells seen in BR8 cells all showed direction selectivity compensation in both eyes.

Apart from the layer V cells very few of the binocular units recorded from group MR animals were direction selective where a cell was defined as being direction selective when the response to movement of the optimal stimulus in the null direction was less than 10% that to movement in the preferred direction (Pettigrew, Nikara and Bishop, 1968). By comparison most of the monocularly driven units were direction selective.

When defined according to this strict criterion the percentage of binocular cells recorded from group BR showing precise direction selectivity was much lower than in the normals. Only 19% of the binocular cells in the BR sample were direction selective compared to 61% of the binocular cells observed in group N. Only one of the animals with both eyes rotated, BR4, showed significantly greater direction selectivity (40%) than the mean for the group (19%). This cat had both eyes rotated in parallel, i.e., the right eye was intorted approximately 60° and the left eye was extorted to approximately 50°. Thus in this animal there was little rotational disparity between the two eyes although there was a vertical disparity of 45° between the two areae centrales. The ocular dominance distribution and receptive field properties apart from direction selectivity for this animal were very similar to the remainder of the group and so have been included in all calculations of means and standard deviations. Overall the majority of the units in the BR sample were bidirectionally selective. See Tables I and II for summaries of all cell properties.

Eye movements

As will be reported more extensively elsewhere, all of the animals with rotations have asymmetrical eye movements most of the time and asynchronous movements less often. In the case of animals such as BR5 with rotations of approximately 90° in both eyes, auditory stimulation to the right of the animal elicited movement in that direction by the right eye and a comparable excursion in the opposite direction by the left eye. Similarly, for auditory stimulation above or below the animal the two eyes responded in opposite directions. In the case of animals with smaller total rotations the eye movements were also nonconjugate. From observations and cinematography of the eye movements, the responses of the two eyes are out of phase to an extent approximately equal to the relative rotation of the eyes. Occasionally the animals appeared to be able to make conjugate eye movements; however, this occurred mainly when animals were making large saccades, apparently to fixate new targets.

Histology

Histological reconstruction of most penetrations were made, verifying that they were in area 17. Gross dissections of the orbit of the eyes of these animals showed surprisingly little scar tissue following surgery. The muscles were tentatively identified on the basis of their innervation pattern, and relative positions of insertion at the back of the orbit. The lateral rectus muscle was assumed to be the muscle whose nerve did not supply other rectus muscles. The three other recti muscles which were innervated by the same nerve, presumably the oculomotor, were assumed to be the medial, superior, and inferior recti. The inferior oblique could also be identified as it has a unique origin in the anteromedial corner of the floor of the orbit adjacent to the lateral aspect of the lacrimal fossa (Duke-Elder, 1973). The muscles appeared to have reattached to the same position on the globe as that to which they attached before rotation. Sperry (1946) described a similar pattern of reattachment in lower vertebrates.

Discussion

The results presented here indicate that under certain conditions neither incongruent visual information to the two eyes due to misaligned visual axes, nor asymmetrical eye movements is sufficient to initiate a loss of binocularity in the developing visual cortex of a kitten.

We have raised 10 cats from the time of natural eye opening with surgical rotation of only one eye (through various angles up to 200^{o}) and found that binocularity is reduced although certainly not abolished, and much less affected than after strabismus. This confirms the earlier studies of Blakemore et al. (1975) and Yinon (1975). Furthermore, there does not appear to be any significant correlations between the angle of rotation and the percentage of binocular units seen in the cortex. The percentage binocularity also shows no obvious relationship to the ability of individual animals to transfer oriented pattern discriminations interocularly. (Compare Chapter II performances and see Fig. 3.)

By contrast electrophysiological recording from area 17 of animals raised with bilateral eye rotations shows them to have approximately normal cortical binocularity despite the misalignment of the visual axes ($10-64^{o}$) and nonconjugate eye movements which were also observed in MR animals. The difference in degree of binocularity of the two groups MR and BR is highly significant and in view of the dramatic effects that selective early visual experience, such as raising kittens, with artificial strabismus either in the light (Hubel and Wiesel, 1965), or in the dark (Maffei and Bisti, 1976), or with alternating monocular occlusion (Hubel and Wiesel, 1965), or when viewing simultaneously disparate orientation information to the two eyes (Hirsch and Spinelli, 1971), has on cortical binocularity, the result is even more surprising.

An immediate explanation for the difference in binocularity is that the MR animals were monocularly deprived and that the BR animals were binocularly blinded. However, this seems very unlikely. The BR animals showed good visual following and visuomotor behavior, whether tested as small kittens or as adults, and they were able to learn visual discriminations without apparent difficulty (Chapter II). Also, very few visually unresponsive cells similar to those found in binocularly deprived animals (Hubel and Wiesel, 1963) were seen in the cortex. However, if we accept that these animals were not binocularly deprived, then it is necessary to assume that the animals developed through the critical period for physiological change of binocular vision (Hubel and Wiesel, 1970; Blakemore and Van Sluyters, 1974) viewing the world through misaligned eyes and that they were constantly receiving incongruent visual information to naturally corresponding points on the two retinae, and still retained cortical connections from both eyes.

It also seems unlikely that the MR group were permanently monocularly deprived since the rotated eye was able to assume domination of the cortex in the two animals (MR1 and MR10) whose normal eyes were sutured shut at 5 and 3 weeks, respectively.

It is possible that, at least for the first week after natural eye opening when the kittens are not making many eye movements with the newly rotated eye, the MR kittens were being monocularly deprived. However, in view of the 61% recovery of the deprived eye's ability to drive cortical neurons that Olson and Freeman (1978) found in animals monocularly deprived for 10 days from day 28-38 and then recorded 29-55 days later, and the almost total recovery (80% binocularity) Ary, Kasamatsu and Pettigrew (1978) have found in animals deprived for a week from days 28-35 and recorded 30 days later, we expect that if the monocular deprivation for the first week is the only cause of binocular breakdown, the MR animals would recover almost normal binocularity. This is probable since in many normal kittens the two eyes may open several days apart suggesting that the first couple of weeks of life are unlikely to be very important in binocular development.

We would now like to reconsider the binocularity of both groups of experimental animals in terms of the three primary physical consequences of rotating an eye--the visual axes of the eyes are misaligned, normal conjugate eye movements are disrupted and at least in the first postoperative week all the extraocular muscles and the afferents from them to the brain are disturbed. The first two effects are permanent. The latter disturbance may only be temporary or it may persist throughout the life of the animal.

Blakemore (1976) has recently reviewed all the types of visual manipulations which are known to interfere with normal visual cortex development and has suggested that the necessary condition for the maintenance of binocularity in cortical neurons is that they should be stimulated by patterned retinal images with contours of approximately the same orientation falling simultaneously on the receptive fields in the two eyes. These conditions are probably met in all our animals, though in the restricted sense of nearly simultaneous activation by different stimuli in different parts of the visual field with different orientations in real space, although these orientations would be comparable if one allowed for the rotation of the visual world. The possibility that this limited degree of binocular synchrony could suffice to preserve cortical binocularity in the BR group seems surprising. However, recent observations on the degree of visual asynchrony permitted indicates that kittens whose visual experience is restricted to stimuli presented alternatively to both eyes with a delay of 1 sec do not lose binocularity while the cortices of animals which are alternatively stimulated with a delay of 4 sec between eyes become monocular (Blasdel and Pettigrew, in preparation).

The fact that the MR group lost binocularity and the BR group did not, suggests that synchronous patterned images are not the only basis for determining binocularity. The angle of misalignment of the visual axes also seems independent of the degree of binocularity of the cortex. Animals MR2 and MR11 with small angles of rotation of one axis did not show significantly greater binocularity than did cats such as MR8 with the largest difference in axis alignment. Also, it is well accepted that independently of the degree of divergence of an artificial strabismus the cortical ocular dominance will be skewed towards monocular (Hubel and Wiesel, 1965).

Animals raised either with artificial strabismus (Hubel and Wiesel, 1965) or with rotation of one eye, or with bilateral rotations, all have appreciable squints and incongruent visual information to the two eyes, but only in the first two groups is there breakdown of cortical binocularity and the breakdown is greater after strabismus than after monocular rotation. This suggests that any interference with the extraocular muscles of one eye has more severe cortical effects than simultaneous manipulation of both eyes but that the magnitude of the effect is not proportional to the degree of muscular interference. Maffei and Fiorentini (1976) also noticed a gradation in disruption of the binocularity of visual cortex of adult cats following monocular or binocular paralysis of the eyes by cutting cranial nerves III, IV and VI which innervate the extraocular muscles. Monocular paralysis produced a breakdown of normal cortical binocularity (binocularity = 40%) whereas the binocular paralysis produced no observable change in the ocular dominance. Possibly monocular paralysis caused some degradation of the retinal image; however as it is known that several months of monocular deprivation after the critical period do not affect cortical ocular dominance, the result is interesting. It suggests that the maintenance of cortical binocularity in our BR animals and in those of Maffei and Fiorentini (1976) is related to the comparable manipulations to the extraocular muscles and necessarily to the positional afferents of both eyes.

Several other papers have appeared recently suggesting that visual input may not be the only factor which influences the binocular development of the cortex. Initially Buchtel, Berlucchi and Mascetti (1972) reported that long term denervation of the extraocular muscles of one eye in an adult cat produced a loss of binocularity of the cortical cells. Maffei and Fiorentini (1976) further showed that this change in ocular dominance occurred even if the cats were maintained in darkness following the immobilization of an eye. Then Maffei and Bisti (1976) raised strabismic kittens in the dark and observed that binocularity was also significantly reduced and suggested that this was due to the asymmetrical eye movements produced by cutting one of the extraocular muscles.

However, in view of the fact that the eye movements are mostly nonconjugate in both our experimental groups and yet the BR group still show normal binocularity it would seem unlikely that the ocular dominance changes seen in dark-reared strabismic kittens were entirely due to asymmetrical eye movements as initially proposed by Maffei and Bisti (1976). Rather the imbalance in proprioceptive information which would follow the cutting of one muscle is more likely (Maffei and Bisti, 1976).

The majority of the asymmetrical eye movements seen in all our cats are probably best explained by the apparent reattachment of the muscles to their original position on the globe prior to section. Thus, most of the asymmetrical eye movements are probably due to the same muscles contracting but now in the new orientation of the eyeball. On the other hand the smaller number of asynchronous and conjugate eye movements mean that other patterns of muscle contraction and hence extraocular afferent activity are present at times in all experimental animals. In the case of the MR animals there would be a definite time, albeit short, after surgery when the extraocular afferents and possibly the pattern of motor corollary discharges (Sperry, 1950) from the extraocular muscles of the two eyes would be very different. Whether the extraocular afferent information would continue to be noncongruent after the muscles of the rotated eye reattach is hard to assess. By comparison the extraocular afferent information from the BR cats would always be more balanced, both in the interim when the muscles were reattaching and after the event since both eyes were rotated, and particularly if the angles of rotation for the two eyes are comparable as is the case in most of our animals. The monocular and binocular immobilization of Maffei and Fiorentini (1976) can also be explained in similar terms. The extraocular afferent information would always be unbalanced in the animals with monocular paralysis and always symmetrical in the animals with binocular paralysis.

Although all the animals, both kittens and adults with monocular rotations and young animals with binocular rotations, studied in our behavioral experiment (Chapter II) showed good visuomotor adaptation to the surgically rearranged visual information, we have not been able to identify many changes in receptive field characteristics of the cortical neurons. The only group of cells to show any significant plastic changes were the binocular layer V corticotectal cells seen in the MR animals with the larger angles of orientational disparity between their visual axes and in BR8 which also had a combined disparity of 90° between the axes. Five cells out of the group of ten binocular cells with the properties described by Palmer and Rosenquist (1974) that we examined in the MR series showed a significant shift in direction preference, such that the receptive fields drawn through both eyes came to have the same direction preference despite almost orthogonal visual axes of the eyes. The four binocular corticotectal cells seen in BR8 also showed similar adjusted direction selectivity.

We have not seen comparable changes in direction selectivity in the other BR animals; however, as the rotational disparities of most of the other animals was approximately 180° this is not surprising. Most of the binocular cells were bidirectional with a very low percentage of strictly directionally selective units, 19% compared to 67% in our normal group.

The receptive field characteristics of most of the cells recorded in both MR and BR animals resembled those initially described by Blakemore, Van Sluyters, Peck and Hein (1975) for animals with monocular rotations. A stable pattern of retinotopic correspondence was maintained by the receptive fields of the neurons examined. The preferred orientations of the binocular cells in the MR and BR animals were comparable for both eyes in terms of retinal coordinates although the standard deviations of the distributions of orientational disparities for binocular cells was much greater for both experimental groups than that for the normal cats (see Figs. 7A and B). A similar spread of orientation disparities is seen in the binocular cells of reversed suture animals (Blakemore and Van Sluyters, 1974). The orientation tuning of individual cells in both experimental groups was also broader than the tuning in the normal group (Fig. 6). Similar observations were originally reported by Blakemore et al. (1975) for their monocular rotations and by Kratz and Spear (1976) for binocularly deprived cats. The fact that none of the animals raised with unilateral rotation, bilateral rotation, reversed suture or binocular deprivation ever receive synchronous aligned visual information to the two eyes during the critical period and that the preferred orientation disparities and tuning range for individual neurons show greater than normal variability seems to suggest that precisely aligned visual stimulation is necessary for the normal development of binocular cells with fine tuning for orientation (Blakemore and Van Sluyters, 1974) in addition to the maintenance of inputs from both eyes onto individual neurons of striate cortex, as has been suggested (Hubel and Wiesel, 1965; Stent, 1973).

The lack of orientation adjustment demonstrated by all our cats stands in apparent contradiction to the recent study of Shinkman and Bruce (1976) who reported a high correlation between the distribution of interocular differences in orientations of binocular cells and the angle of prism rotation ($\pm 16^{\circ}$, 8° per eye) experienced during early development. We do not have an immediate explanation.

Possibly the contradiction rests on the intrinsic difference of giving an animal rotationally disparate binocular experience through surgery or with prisms.

In conclusion, our experiment indicates that neither misaligned visual input nor asymmetrical eye movements alone initiate a loss of cortical binocularity. Rather our results suggest that aligned, congruent visual information to the two retinae is more necessary for the development of cells with normal fine tuning for orientation than for the maintenance of binocularity. It would also appear that comparable manipulations to the two eyes, in this case bilateral rotations, have less drastic effects on cortical binocularity than does monocular rotation. We suggest that the apparently normal ability of both eyes to drive cortical neurons in animals with large binocular rotations is due to the intermittent quasi-synchronous visual stimulation of the same cortical neuron through each eye by random stimuli of approximately the same orientation in terms of retinal coordinates, and to the continued presence of balanced afferent information from the extraocular muscles of both eyes to the brain.

The observations that some of the corticotectal cells in layer V of animals with both monocular and binocular rotations show significant readjustment of the direction preference of the rotated eye to concur with that of the normal eye suggests that perhaps more physiological evidence for the behaviorally observed visuomotor adaptation to the displaced visual field may be found in the superior colliculus of these animals.

CHAPTER IV

A Role for Extraocular Afferents in Post-Critical Period Reversal of Monocular Deprivation[1]

Introduction

Electrophysiological experiments have shown that synaptic connections in the kitten visual cortex in the first 3 months of life are highly susceptible to the effects of visual deprivation. Manipulation of the visual input by lid suture leads to a marked decline in the ability of that eye to drive cortical cells (Wiesel and Hubel, 1963, 1965; Hubel and Wiesel, 1970). On the other hand, after this critical first 3-month period, the ability of a cat to recover from the effects of deprivation or to be affected by lid suture is severely limited (Hubel and Wiesel, 1970). The synaptic connections appear to be much less flexible in an adult cat in that similar 3-month periods of eye suture produce no obvious change in binocularity of the cortex (Hubel and Wiesel, 1970; Wiesel and Hubel, 1965).

The conclusion that synaptic plasticity is limited to the first 3 months of life is supported by experiments with reverse lid suture where the kitten is forced to use the previously closed eye (Blakemore and Van Sluyters, 1974; Blasdel and Pettigrew, 1978).

In contrast, there are a number of recent experiments indicating that synaptic changes are possible in the visual cortex after the 3-month critical period. For example, Buchtel, Berlucchi and Mascetti (1972) found that long-term denervation of the extraocular muscles of one eye in a normal adult cat produces a loss in binocularity of cortical cells. Maffei and Fiorentini (1976) further showed that

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[1] This work has been submitted for publication in J. Physiology (London) by D. P. Crewther, Sheila Gillard Crewther, and J. D. Pettigrew.

this effect was not due to alteration of the visual input as might have been suspected from previous experiments (Hubel and Wiesel, 1965) but due to the paralysis of the eye muscles, since the change in ocular dominance occurred even if the animals were maintained in darkness following the immobilization of an eye.

More recently it has been found that the effects on the visual cortex of monocular deprivation during the critical period can apparently be reversed in adult cats, in just a few hours following enucleation of the experienced eye (Kratz, Spear and Smith, 1976). The experiments of both the Italian group and of Kratz et al. (1976) involved disturbance of other inputs besides the visual one and the possibility that these two post-critical period phenomena might be linked was suggested to us by the fact that pressure blinding of the experienced eye of a monocularly deprived cat does not produce the changes observed by Kratz et al. (1976) following enucleation. Pressure blinding yields only a very small proportion of neurons driven by the deprived eye (Blakemore and Hillman, 1977; Harris and Stryker, 1977) in contrast to the large numbers seen after enucleation. We wondered whether the difference might be attributable to the removal of extraocular afferents which would be an inevitable part of the latter procedure, but not of the former.

The present findings support this interpretation since they indicate that combined pressure blinding of the retina and retrobulbar block of the extraocular afferents does bring about a reversal of ocular dominance of the cortex contralateral to the deprived eye, while either procedure by itself is ineffective.

Methods

Animals and rearing conditions

Six monocularly deprived cats were used in this experiment. The right eyelids of two of the cats (CPROP V and CPROP VI) were sutured at the time of normal eye opening and were respectively 12 and 14 weeks of age on the day of recording, when the sutured eyelid was opened. The other 4 cats all had their right eyelids sutured at 5 weeks of age and remained so until the day of recording. CPROP III and IV were from the same litter and were 19 months old when used. CPROP I and VII were over a year old. All kittens were housed with their mothers in large individual cages until after weaning. After this, the kittens were moved to the main colony room and maintained in constant temperature and 18 hr light/6 hr dark conditions until the date of recording.

Surgery and preparation

Eyelid suture operations were performed under 1-2% fluothane in 2:1 N_2O/O_2 anesthesia. Routine daily checks were made to ensure that any windows which might develop between the lids were repaired immediately. Infection in the eyes was controlled by topical applications of ophthalmic Furacin-Penicillin gel or Gentocin solutions. The tracheotomy and cephalic vein cannulation were done under the same gaseous anesthetic. The cats were then transferred to the stereotaxic apparatus and paralyzed with a loading dose of 40 mg of Flaxedil (gallamine triethiodide) intravenously. A constant i.v. infusion of 10 mg/kg/hr Flaxedil and 10% dextrose solution in normal saline was begun immediately. The animal was artificially respired with 80% N_2O and 20% O_2 during craniotomy. Throughout the recording session the gas ratio was maintained at 75% N_2O, 22.5% O_2, and 2.5% CO_2. In all animals the crown of the postlateral gyrus in the hemisphere contralateral to the deprived eye was exposed. Kratz et al. (1976) indicated that the percentage of cells driven by the deprived eye, following enucleation, was greater in the contralateral than in the ipsilateral hemisphere. All areas of incision were covered in 2.5% xylocaine jelly and topical antibiotic.

The electrocardiogram was recorded with electrodes across the animal's chest and followed continuously with an audio monitor. No changes in heart rate were observed during the pressure blinding. The temperature was maintained at 37°C by an electric blanket in a feedback loop with a rectal thermometer. The deprived eye was dilated with 1% Cyclogyl and the nictitating membranes withdrawn with 2.5% phenylephrine (Neosynephrine). No mydriatic agent was used on the nondeprived eye so that we could monitor the retrobulbar block by watching the pupil. An ophthalmoscope with a very bright quartz halogen lamp was used to project a reflected image of the position of the optic disc and area centralis for each retina on the tangent screen at 57 cm (Fernald and Chase, 1971). Contact lenses of zero power (7-9 mm radii of curvature) were used to protect the corneas. We chose the size of contact lens which produced the sharpest focus of the image on the tangent screen.

Animals were routinely injected intramuscularly with 20,000 units of a general wide spectrum antibiotic, and with 1 mg of dexamethazone at the beginning of each recording session. The recording sessions lasted for two days.

Pressure blinding and retrobulbar block

A 20 gauge 1.5 inch catheter placement unit (Cathlon IV) was inserted through the sclera into the posterior chamber of the eye. The unit was angled backwards to avoid damaging the lens. The needle was then withdrawn so that the outer teflon catheter could be connected to an adjustable column of mammalian Ringers solution and to a mercury manometer which measured the pressure in the eye.

The blockade of retinal ganglion cell activity was established by raising the column of liquid approximately 2 meters, which produced an intraocular pressure greater than the systolic blood pressure (120-140 mm Hg) (Bornschein, 1958a,b) and hence prevented further blood flow to the retina. This was observed directly with an ophthalmoscope. It should be noted that repeated pressure blinding eventually caused bleeding into the vitreous of the posterior chamber of the eye and hence after several reversible blindings, the eye could transmit only diffuse images at best. In several animals the retina of the treated eye was detached from the choroid at the time of postmortem.

The retrobulbar block was produced by inserting another catheter placement unit far back into the posterior region of the orbit near the apex of the muscle cone, usually on the temporal side, and injecting either 2% Carbocaine or a 5% Xylocaine in 7.5% glucose solution. The ciliary nerve which controls pupil constriction runs with the oculomotor nerve from the brain to the orbit, and passes alongside the opthalmic branch of the trigeminal which contains most of the extraocular afferents, including the majority of the proprioceptors (Whitteridge, 1953; Batini and Buisseret, 1974). Hence we assumed that sufficient anesthetic to block ciliary nerve action and cause total pupil relaxation was also sufficient to block the other extraocular afferents. About 0.2 ml of 5% Xylocaine was sufficient if the cannula was correctly placed. Sometimes the pupil dilated immediately and at other times the relaxation developed gradually over 5-10 min.

In several cases we saw dilation of only one half of the pupil initially. Relocating the cannula within the orbit or else injecting more local anesthetic from the nasal side produced total dilation. During the period referred to in the results as retrobulbar block, local anesthetic was reapplied whenever the pupil began to constrict. Reapplication of local anesthetic was usually necessary from 2 to 5 hr after initial application.

A direct surgical approach to the extraocular afferents appears feasible for those located in the superior part of the orbit. However, we report here only results obtained with the indirect approach to these afferents using retrobulbar block, since by this method, the afferents from the inferior orbit can be blocked at the same time, and without surgical damage.

Recording methods and visual stimulation

A small plastic chamber was cemented to the skull around the area of the craniotomy, and a tiny hole was made in the dura through which the microelectrode was introduced. After the electrode was in place the cortex was stabilized by pouring agar around the electrode in the chamber and then by sealing the entire well with a covering of wax. A custom-built stepping motor micromanipulator was used to advance the electrode up or down in discrete steps of 1 μm or more.

We used Levick-type tungsten-in-glass microelectrodes (Levick, 1972). The dimension of the exposed tungsten tip was 10-15 μm and 2 μm diameter at the exit from the capillary. The signal from the electrode was first fed into a conventional high impedance preamplifier and from there to an oscilloscope for observation of spike waveforms. The response discharges were also played through an audio monitor. Additional circuitry was available for converting the nerve cell spikes into pulses accepted by a minicomputer (NOVA 2) for immediate playback or for storage and later analysis. Preliminary receptive field plots were always done by hand.

Electrode penetrations were made in striate cortex, down the medial wall of the postlateral gyrus in or near the area centralis projection. A single long penetration was made in each of the first 5 cats. In CPROP VII a second penetration was also made. The tracks were angled between 7° and 15° anterior and between 5° and 10° medial to increase the probability of crossing many ocular dominance columns (Hubel and Wiesel, 1962, 1963, 1970). Action potentials thought to arise from cell bodies were distinguished from nerve axon spikes by the waveform criteria described by Bishop, Burke and Davis (1962). The present results only refer to cell recordings.

Visual stimuli were presented on a rear projection screen 57 cm from the nodal point of the eye by a custom-built projector which allowed joystick control of position, orientation and size of the light slit. The stimulator was wired into the computer system so that stimuli could be manually and automatically presented. Background illumination was maintained in the mesopic range and the light slit was 1-2 log units brighter. As the electrode was advanced a visual noiseboard was used to activate units which were not firing spontaneously.

Histology

A series of microlesions was made by passing an 8 μA current (negative at the electrode) for 5-10 sec at several depths in each penetration.

The animals were given a greater than surgical anesthetic dose of Nembutal and were then perfused through the heart with isotonic saline followed by 10% formalin in saline. A block of the brain was taken from the region of the penetration and then cut into a series of 40 μm sections on a freezing microtome. Sections were stained with cresyl violet. The border of areas 17/18 was defined

(Otsuka and Hassler, 1962) and the track reconstructed from the electrolytic lesions. Track lengths given in the results refer to passage through grey matter only.

Results

We recorded from at least ten cells in each track to document the effects of monocular deprivation (M.D.) alone before applying either type of blockade. Of the 89 units thus recorded, 75 were driven by the experienced eye, 4 were driven by the deprived eye, and 10 were unresponsive. The total length of track involved was 6.3 mm corresponding to an average of 71 μm between cells studied.

The results from the three types of experiments performed, that is, response to pressure blinding alone, response to retrobulbar block alone, and response to combined pressure blinding and retrobulbar block are presented below under separate headings. The details of two specific experiments, CPROP V and CPROP VI, are shown in Figs. 1 and 2.

Pressure blinding alone (P.B.) N = 71

In two cats, the normal eye was pressure blinded for a long time (15 hr for CPROP III and 8 hr for CPROP V) resulting, most probably, in the death of the retinal ganglion cells from anoxia. We examined two of the eyes after perfusion and found that the retinas were totally detached from the choroid. Of the 71 cells studied only three were responsive to visual stimulation of the deprived eye. This is well within the accepted (0-7%) bounds for a monocularly deprived but otherwise normal cat (Wiesel and Hubel, 1965). The 68 cells comprising the remainder of the sample were identified by their maintained activity although they were unresponsive to stimulation of either eye. Tests for orientation and velocity selectivity, stimulus size, flash response and preference for light or dark stimuli were carried out on all of the unresponsive cells with negative results. The total

Fig. 1. A single electrode track through the left area 17 of a monocularly deprived cat CPROP V (right eye closed for weeks 1-12) shows the effects of pressure blinding (P.B.) and retrobulbar blockade (R.B.) applied to the experienced (left) eye. The position of all units encountered along the track is shown at left in relation to the depth below the cortical surface (in m.m.). There are more units in this column than the sum of the unresponsive (Unresp) and responsive (Resp) cell columns because at least 15 min of testing is required to classify a unit, and a number were not held this long.

Ocular dominance (O.D.) groups from 1 (exclusively contralateral) to 7 (exclusively ipsilateral) follow the convention of Hubel and Wiesel (1962). All units encountered before manipulation of the experienced eye, were dominated by this eye. While responsiveness to the experienced eye was abolished neither reversible (short bars under P.B. column), nor continuous pressure blinding had a significant effect on the responsiveness of units of the deprived eye. (The single unit at depth 1.8 mm responsive to the deprived eye was located in layer IV where a small number of such cells are to be expected.) The introduction of retrobulbar blockade (column under R.B.) led to a significant increase in the proportion of units which could be driven by the deprived eye (O.D. group 1). That this effect was not due merely to the passage of time after pressure blinding was ascertained in other experiments (CPROP I and CPROP VII) where the retrobulbar block was instituted first and where pressure blinding led, within 17 min, to units responsive to the deprived eye.

CPROP V

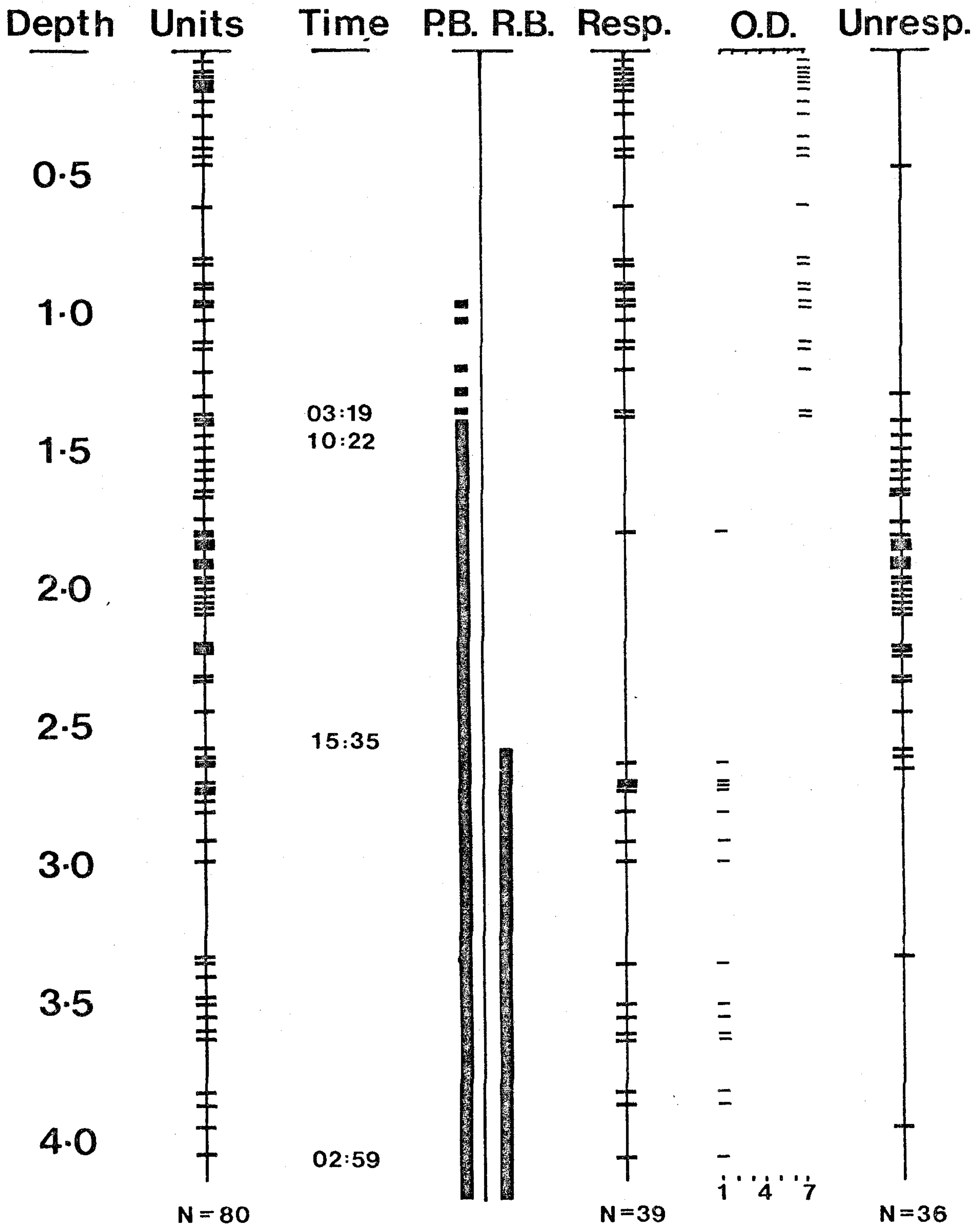
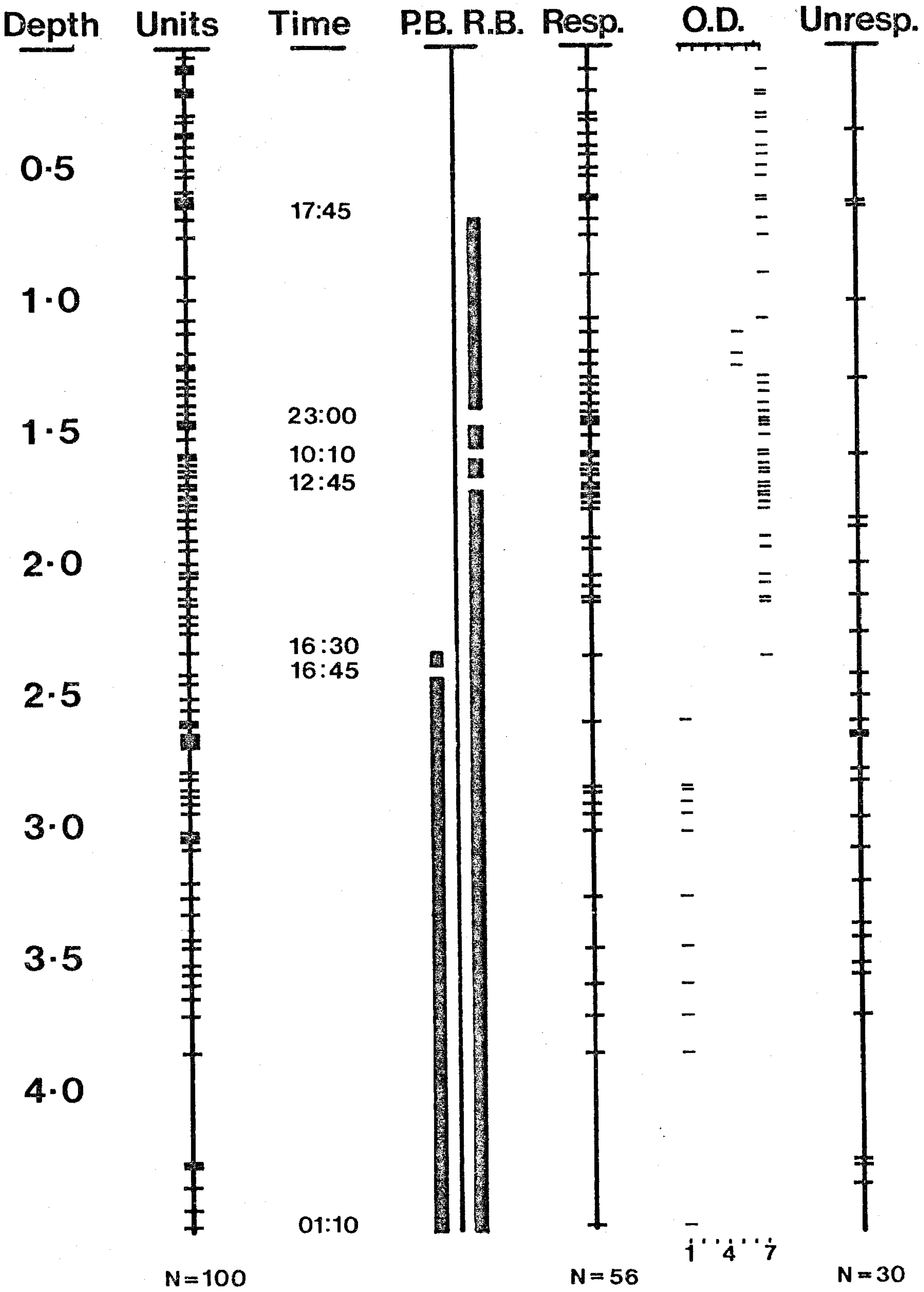

Depth
Units
Time
P.B. R.B.
Resp.
O.D.
Unresp.
0·5
1·0
1·5
2·0
2·5
3·0
3·5
4·0
03:19
10:22
15:35
02:59
1 4 7
N=80
N=39
N=36

Fig. 2. An experiment similar to that shown in Fig. 1 (same conventions) except that the order of manipulations was reversed. The introduction of retrobulbar blockade (R.B.) alone had no effect upon the responsiveness of units to the deprived eye. After the introduction of pressure blinding (P.B.) a significant number of units were found which could be driven by the deprived eye. Taken together with the results in Fig. 1 which shows that pressure blinding alone has no significant effect, these results indicate that both optic nerve and extraocular nerve activity must be blocked to promote a return of responsiveness to the deprived eye. The remaining possibility, not entirely eliminated by Figs. 1 and 2, that responsiveness of the deprived eye is a function of depth in the cortex was ruled out in an experiment (CPROP VII) in which both manipulations (P.B. + R.B.) were instituted at the start of the electrode track. High proportions of units responsive to the deprived eye were found throughout the track.

CPROP VI


Depth
Units
Time
P.B. R.B.
Resp.
O.D.
Unresp.
0·5
1·0
1·5
2·0
2·5
3·0
3·5
4·0
17:45
23:00
10:10
12:45
16:30
16:45
01:10
1
4
7
N=100
N=56
N=30

length of track involved was 3.7 mm corresponding to a sampling frequency of 1 cell per 59 microns which is similar to that seen under the control monocularly deprived (M.D.) condition.

Thus, in agreement with Blakemore and Hillman (1977) and Harris and Stryker (1977), we find that permanent pressure blinding alone does not produce a significant change in the percentage of cortical cells driven by the deprived eye.

Short-term pressure blinding (from 5 to 8 min) was also tried (prior to the permanent blinding) but with little effect on the 8 cells studied. Within 30 sec of the time when the pressure in the experienced eye was increased to a level greater than the systolic blood pressure of the cat (120-140 mm Hg) all response to visual stimulation of the experienced eye ceased. Upon lowering the intraocular pressure of the experienced eye to normal there was a noticeable reduction of the spontaneous activity of the cell within the first minute, followed by a sporadic responsiveness to visual stimulation of the experienced eye within 3-4 min when we also noticed a gradual return of the spontaneous activity. The cell required a rest period between stimulations for the next 5-6 min, and full restoration of the response only occurred after about 10 min.

Retrobulbar blockade alone (R.B.) N = 59

A local anesthetic block of the nerves supplying the extraocular muscles passing through the apex of the orbit (retrobulbar block) was induced in 3 cats, CPROP I, CPROP IV, and CPROP VI, using 5% Xylocaine or 2% Carbocaine solutions, before any pressure blinding was attempted. Of the 59 units studied in these 4 experiments, 41 were driven solely by the experienced eye, 5 were binocular to some extent, and 13 were unresponsive. The unresponsive units appeared at random intervals along the penetrations.

Three of the 5 binocular units occurred in CPROP VI soon after the administration of additional anesthetic to maintain the block. They were characterized by a very weak response to stimulation of either eye. It was suspected that these binocular units may have arisen due to partial anesthetization of the optic nerve, because of the noticeable reduction in the background cortical response to stimulation at this time. For this experiment on the effect of retrobulbar block alone, the sampling frequency was 1 cell per 54 microns and the total length of track involved in this sample was 3.2 mm, from 4 animals which should have guaranteed the passage through several ocular dominance columns.

Combined retrobulbar blockade and pressure blinding (P.B. + R.B.) N = 118

In 3 animals (CPROP I, CPROP IV, and CPROP VI) the retrobulbar block was followed by pressure blinding for a long period. In each of these experiments significant numbers of neurons were found which could be driven by the deprived eye following both treatments. In the case of CPROP I, units with reliable receptive fields in the deprived eye were seen within 17 min of raising the intraocular pressure of the nondeprived eye. These cells were seen in the top layers of the cortex, as were those seen at the beginning of the second penetration in CPROP VII where the two treatments were introduced together.

In CPROP V a retrobulbar block was established after the retina had been continuously pressure blinded for 5 hr. Over the next 11 hr, 15 out of the 20 units examined were responsive to stimulation through the deprived eye. As these cells did not appear to be significantly different from those seen in the first 4 experiments where the order of retrobulbar and pressure block was reversed, we have grouped the data together.

A total of 118 cells was studied in the 5 animals. Of these, 64 were driven by the deprived eye and 54 were unresponsive; that is, 54% of the cells encountered in this category were responsive to stimulation of the deprived eye. The properties of the cells are given in the next subsection.

The comparison of responsiveness to the deprived eye between the combined treatment sample (54%) and the monocularly deprived (M.D.) sample (4%) is especially significant since the same cats were used in gathering most of the data for the two samples. The average cell spacing was the same for both samples (71 μm) and the total track lengths were also comparable (6.3 mm for the M.D. sample versus 8.4 mm for the combined P.B. + R.B. sample).

The results of the 3 experiments with pressure blinding (P.B.), retrobulbar blockade (R.B.) and the combined treatments (P.B. + R.B.) are summarized in Fig. 3, which shows that recordings following either procedure alone, are not significantly different from recordings in the control monocularly deprived conditions, in terms of the responsiveness of the deprived eye. In contrast, both procedures applied together produce a significant increase in the responsiveness of the deprived eye (to greater than 50% of all units encountered).

In 9 cases it was possible to study the effects of reversible pressure blinding upon a single cell while a retrobulbar block was maintained. The receptive field of each of these 9 cells was first plotted for the experienced eye and some time was spent searching with the appropriate stimulus to determine that there was no response from the deprived eye. The experienced eye was then pressure blinded for periods of up to 7 min after which the intraocular pressure was reduced

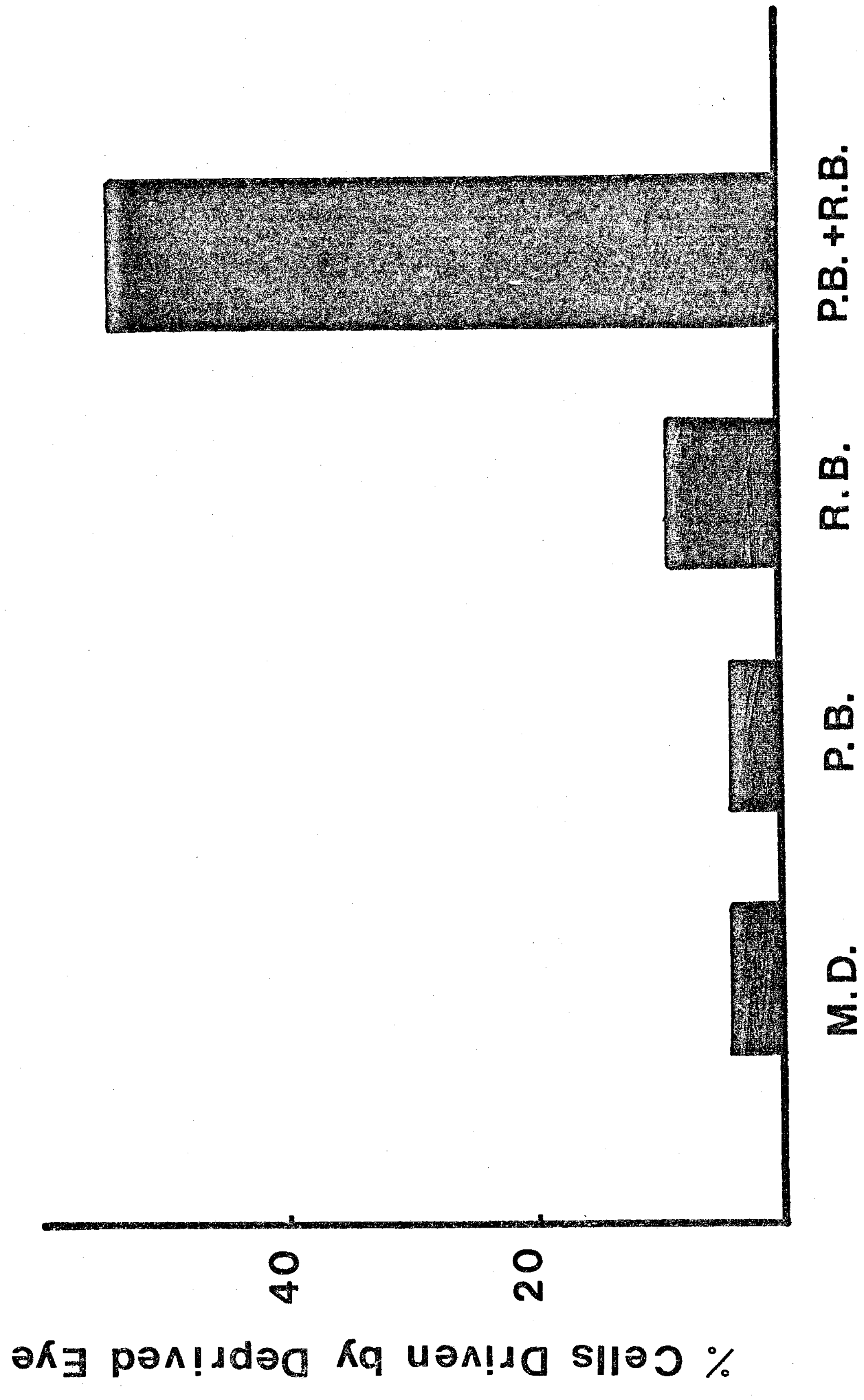
Fig. 3. Pooled data from six monocularly deprived cats showing the proportion of cells driven by the deprived eye in samples from each of the four conditions:

(i) M.D. - Monocularly Deprived. The control M.D. sample of cells was collected at the beginning of each track before any manipulations were performed with the exception of CPROP VII in which two penetrations were made; the first was a long control M.D. track and the second began with retrobular blockade followed immediately by pressure blinding.

(ii) P.B. - Pressure blinding alone. Sample derived from CPROP III which had 15 hr of continuous P.B. of the experienced eye and CPROP V which had 8 hr of P.B. before any retrobulbar block was instituted. Although the data are drawn from only two cats the low proportion of units which show responsiveness to the deprived eye is in agreement with other studies (Blakemore and Hillmann, 1977; Harris and Stryker, 1977).

(iii) R.B. - Retrobulbar block alone. Data derived from 3 animals (CPROP I, CPROP VI, CPROP VI) in which a retrobulbar block was applied for up to 23 hr (in CPROP IV).

(iv) P.B. + R.B. - Combined pressure blinding and retrobulbar blockade. These data are derived from 5 cats in which there was a variation in both the order of application of the treatments (P.B. first in 2 cats; R.B. first in 2 cats and in one cat, CPROP VII, the R.B. was introduced at the top of the second penetration and followed immediately by P.B.) and the depth in the cortex and stage of experiment at which they were introduced. The high proportion of units driven by the deprived eye was found in all cases of combined treatment and contrasted greatly with the low proportion found following either treatment alone.


% Cells Driven by Deprived Eye
40
20
M.D.
P.B.
R.B.
P.B.+R.B.

to normal again. The cortical response from the experienced eye disappeared approximately 20-30 sec after the pressure was applied. Three minutes later, a sporadic firing was observed in 4 of the 9 cells studied, and an excitatory receptive field area could be mapped in response to stimulation of the deprived eye over an area of 5°-10° in diameter. While the response was clear the receptive fields did not have well defined boundaries nor were any specific cell properties observed. Upon removal of the pressure block there appeared to be an increase in responsiveness to the deprived eye within the first 30 sec, followed by a period of up to 1 min when visual stimulation of either eye would elicit a response. After 3-5 min the response of the deprived eye disappeared and once again only the experienced eye could drive the units though in an abnormal fashion with waxing and waning of the response. Normal response of the cortical cells to stimulation of the experienced eye returned approximately 10 min after the pressure was relieved.

Receptive field characteristics of cells responsive to the deprived eye

Of the 64 cells driven by the deprived eye under the condition of combined pressure blindness and retrobulbar block, 42 (66%) had very well defined receptive fields, 16 (25%) had fields with less precise boundaries, while 6 (9%) were only very weakly responsive. The receptive field core sizes (Pettigrew, Nikara and Bishop, 1968) for the 42 cells were on the average, somewhat larger than those for the M.D. sample of cells; a mean of 3.6° on the retina with a standard deviation of 2.1° for the P.B. + R.B. sample compared with a mean of 2.1° and a standard deviation of 1.7° for the M.D. sample.

In general, though most of the fields were well defined, the properties of direction, orientation and velocity selectivity were often absent. In a few cases the receptive fields were not well defined but the units showed direction or orientation selectivity. Of the 64 cells studied, 30 (47%) were found to be direction selective, 13 (20%) were orientation selective (as assessed by comparing the response to a spot stimulus with that of a bar stimulus) and 4 (6%) were velocity selective. This compares with 39% direction selective and 12% orientation selective as found by Kratz et al. (1976). Fourteen (22%) of the cells showed a response to a flashed stimulus, but usually this response could be elicited uniformly over the field; only 4 cells had receptive fields with specific subregions that showed separate ON and OFF responses. Rapid habituation to a stimulus was seen in 22 (34%) of the cells (compared with 38% of Kratz et al., 1976).

Of the 42 cells which possessed well defined fields 22 were direction selective and of these 8 were orientation selective as well. Five of these direction and orientation selective cells also showed a flash response and 4 of them were designated as simple cells. The other unit was classified as complex as its flash response was uniform throughout its receptive field. Five more units had properties normal enough to be defined as complex cells (Hubel and Wiesel, 1962, 1963).

The properties of all cells driven by the deprived eye, including the 12 units in the M.D., P.B. and R.B. categories are shown in Table I.

Two interesting classes of cells outside the normal categories were observed. In one class, 6 cells driven by the deprived eye were characterized by a very high level of spontaneous activity which was tonically inhibited by a moving stimulus of any form placed over part of the field. The tonic inhibition tended to habituate unless the stimulus was continuously agitated within the inhibitory areas. The receptive fields of this group averaged about 4° in diameter.

Table I. Properties of cells driven by the deprived eye under the four conditions: M.D. - monocularly deprived, P.B. - pressure blinding, R.B. - retrobulbar blockade, P.B. + R.B. - combined pressure blinding and retrobulbar blockade. The table documents the number of cells in each sample (including cells unresponsive to stimulation of either eye) and compares the number of cells responsive to deprived eye stimulation, the average cell spacing, and the various stimulus characteristics of the cells driven by the deprived eye: well defined receptive field boundaries, direction and orientation selectivity, habituation to successive stimulation presentations, response to a flashed stimulus, and velocity selectivity. Of the 42 cells in the (P.B. + R.B.) category which possessed well defined receptive fields, 22 were direction selective and of these 8 were orientation selective as well. Ten cells had properties normal enough to be classified according to the conventions of Hubel and Wiesel (1962). Four units were designated as simple and six as complex cells. It is apparent from this table that retinal inactivation of the experienced eye by pressure blinding (P.B.) produces a very different cortical effect from that seen after inactivation of all afferents, visual and extraocular, by combined pressure blinding and retrobulbar blockade (P.B. + R.B.).

TABLE I

	Number of Cells	Resp.	Cell Spacing (microns)	Properties of Cells Driven by the Deprived Eye					
				Good Field Definition	Direction Selectivity	Orientation Selectivity	Habituation	Flash Response	Velocity Selectivity
M.D.	89	4	71	2	2	2	0	2	2
P.B.	71	3	59	0	0	0	0	0	0
R.B.	59	5	54	1	1	1	0	1	1
P.B. + R.B.	118	64	71	42	30	13	22	14	14

The other group of 11 cells resembled those found in immature cortex or in the cortex of binocularly deprived animals (Hubel and Wiesel, 1965; Pettigrew, 1974; and Blakemore and Van Sluyters, 1975). These units had well defined fields but no direction or orientation selectivity and no flash response. They responded to a wide range of stimulus velocities.

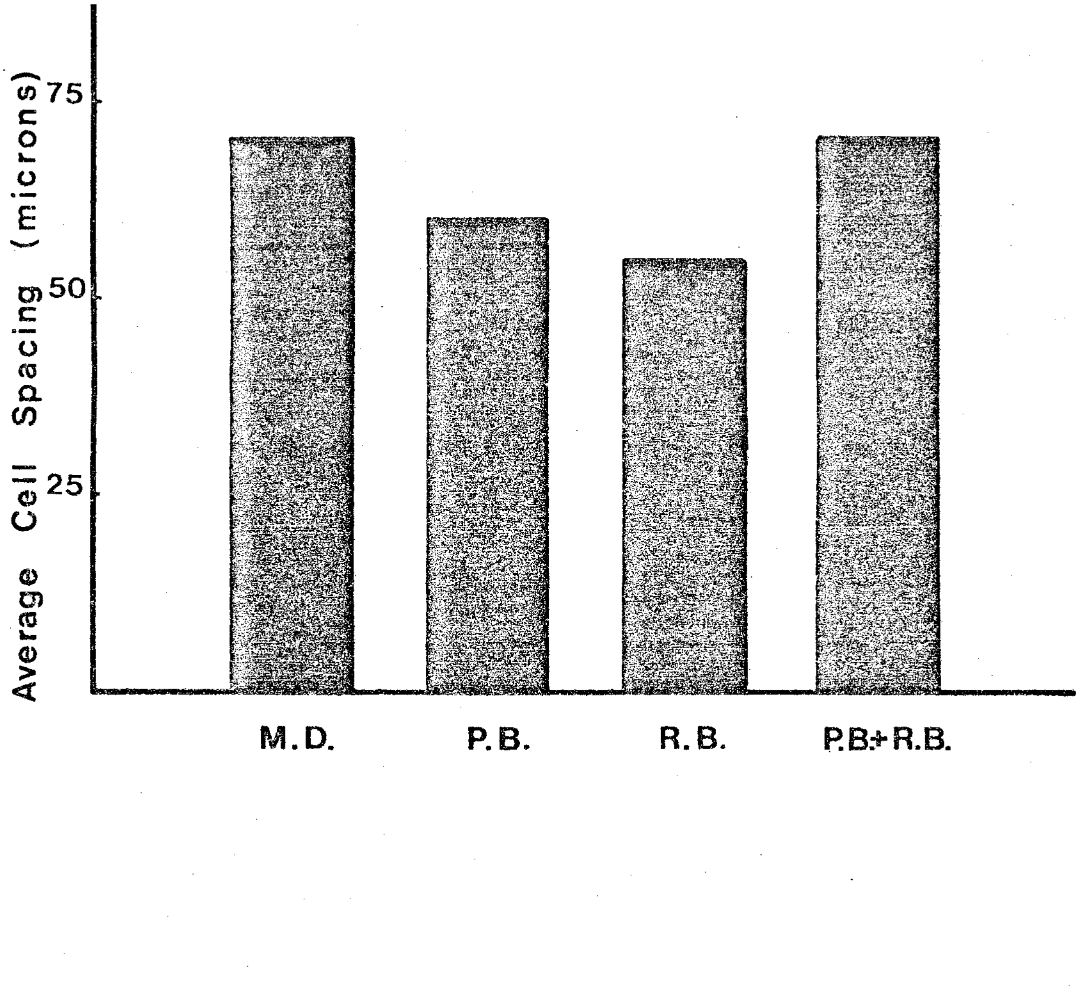
In all, 64 cells out of the sample of 118 units (i.e., 54%) seen after combined optic nerve and extraocular nerve block, were responsive to stimulation through the deprived eye, which compares with the 31% of cells seen by Kratz *et al.* (1976) after enucleation. The greater responsiveness of our sample may be due to the fact that all our penetrations were made contralateral to the deprived eye. Kratz *et al.* (1976) examined the effects of enucleation on both the ipsilateral and contralateral cortices and reported that the ocular dominance shift was greater in the latter.

We found little evidence for clustering of responsive cells, either in terms of the alternation between responsive and unresponsive cells (Kratz *et al.*, 1976) or in terms of local increases in cell density. A comparison of the average spacing between units encountered in the 4 procedures demonstrated no significant difference and is illustrated in Fig. 4. The slight increase in cell density for the R.B. sample (54 μm) as compared with the other samples may be attributable to the greater proportion of this track in layer IV.

Histology

Histological reconstructions have been made of the electrode tracks of all 6 animals. The penetrations in CPROP I, CPROP III, CPROP IV, CPROP V, CPROP VI and CPROP VII were all localized within the grey matter of area 17.

Fig. 4. Represents the average distance between cells encountered (either responsive or unresponsive) in the seven penetrations under the conditions: no treatment of the experienced eye (M.D.), pressure blinding of the experienced eye (P.B.), retrobulbar blockade (R.B.), and combined pressure block of the retinal output of the experienced eye and a retrobulbar block of its extraocular afferents (P.B. + R.B.). The actual distributions of cell spacing are broad (partly due to laminar differences in cell density) and overlap greatly. The similar cell densities in the four categories are not consistent with explanations which base the increased numbers of units obtained in the (P.B. + R.B.) condition upon sampling biases or simple changes in the general level of excitation of the cortex. Instead these sampling densities support the hypothesis of increased specific responsiveness of the cortex to the deprived eye, and extend the results obtained with reversible pressure blinding in the presence of retrobulbar block where individual neurons were shown to have potentially functional connections to the deprived eye which would be revealed electrophysiologically by silencing the connections from the experienced eye.


Average Cell Spacing (microns)
75
50
25
M.D.
P.B.
R.B.
P.B.+R.B.

After track reconstructions we found 18 of the cells (28%) driven by the deprived eye to be in layer IV, 12 (19%) in layers II and III and 34 (53%) were in layers V and VI. There did not appear to be any unusual correlations between cell number or type found and lamination of the cortex.

Discussion

The findings reported here indicate that, to produce a reversal in the ocular dominance of the cortex contralateral to the deprived eye of a cat monocularly deprived (M.D.) throughout the critical period, it is necessary to eliminate both the output of the retina and the extraocular afferents of the experienced eye.

The contribution of the extraocular afferents appears to account for the fundamental difference between the effects of pressure blinding and the effects of enucleation. Pressure blinding of the retinal ganglion cells of the normal eye was insufficient to reverse the cortical effects of long-term deprivation even over a period of 15 hr. Blakemore and Hillman (1977) and Harris and Stryker (1977) have all reported similar negative results for pressure blindings. We therefore conclude that the ocular dominance shift seen after enucleation by Kratz et al. (1976) does not depend on the removal of optic nerve output alone.

A different interpretation is preferred by Harris and Stryker (1977), who contend that the increase in responsiveness of the deprived eye is only an apparent one resulting from the reduction in background activity produced by silencing the output of the experienced eye. Since such an interpretation is based upon the assumption that optic nerve blockade and enucleation have equivalent effects, we cannot agree with it. In fact, the data of Harris and Stryker (1977) also show a difference between the effects of pressure blinding and enucleation.

They found the latter procedure resulted in one third of the cells encountered being responsive to the deprived eye, while the former treatment produced little change in the ocular dominance. Our own data on this point were even more striking since the comparison can be made in the cortex of the same monocularly deprived cat where pressure blinding alone had no significant effect on responsiveness of the deprived eye. Introduction of a retrobulbar block after permanent pressure blinding of the experienced eye produced a significant shift in the ocular dominance of the contralateral cortex similar to that seen after enucleation (see Fig. 1, CPROP V). The qualitative and quantitative similarity in receptive field properties between the cells driven by the deprived eye after the combined treatments and the cells described by Kratz et al. (1976) suggests that pressure blinding and retrobulbar block together mimic the effects of eye enucleation rather well.

Our results also suggest that at least half of the cortical cells in monocularly deprived cats have synaptic connections from the deprived eye which are not normally seen with electrophysiology. Under normal M.D. conditions Stryker and Shatz (1976) found the majority of cells driven by the deprived eye to be in layer IV. However after histological reconstruction of our penetrations we found less than 30% of the cells driven by the deprived eye to be in layer IV. The other 70% were spread through layers II, III, V and VI.

A small number of cells, 4 out of the group of 9 upon which we performed the experiment, was found with connections to the deprived eye which could only be demonstrated during reversible silencing of the connections from the experienced eye. In the presence of a retrobulbar block alone, these units were exclusively driven by the experienced eye. About 3 min after the intraocular pressure was raised, stimulation of the deprived eye elicited a weak but definite response from the cells. When the pressure was relieved the ocular dominance of the cells reverted to the experienced eye after a brief period, during which excitatory regions could be mapped for both eyes.

The hypothesis that many cortical cells in a monocularly deprived cat have synaptic connections with both eyes was originally suggested by the experiment of Duffy, Snodgrass, Burchfield and Conway (1976). These authors were able to elicit shifts in the ocular dominance of 20 out of 33 cortical neurons within 30 sec of low dosage intravenous injections of bicuculline (an inhibitory antagonist) to alert monocularly deprived cats.

Our results suggest an intimate relationship between extraocular afferent input to the brain and the post-critical period reversal of the effects of monocular deprivation on striate cortex cells in cat. The experiments of Buchtel et al. (1972), Fiorentini and Maffei (1974) and Maffei and Fiorentini (1976) also suggest that extraocular afferent feedback is important for maintenance of binocularity in the normal adult cat. A decrease in the number of binocular cortical cells was reported by all these authors following immobilization of one eye.

The indirect nature of our approach to the extraocular afferents, using retrobulbar anesthesia, does not allow us to make any definite statements about the specific afferents involved in the effect. However the only known afferent connections existing between the extraocular muscles and the brain are proprioceptive sensory nerves and pain fibers.

We do not think the reversals we saw after both treatments were merely due to anesthetization of pain fibers as no change in heart rate was observed when the intraocular pressure was raised in the absence of Xylocaine or Carbocaine.

Also, Arden and Söderberg (1961) using cerveau isole and encephale isole animals saw no autonomic changes following pressure blinding.

On the other hand, cortical responses to a stretch of the eye muscles have recently been observed by Daniels (1976, personal communication) and Buisseret and Maffei (1977). The latter authors found that after enucleation, both stretch of the extraocular muscles and stimulation of the intraorbital branch of the motor nerves along which the proprioceptors are known to run (Cooper, Daniel and Whitteridge, 1955) elicited responses with a latency of 25-40 msec from some area 17 neurons. This suggests to us that the pathway taken by these extraocular afferents is polysynaptic and that these proprioceptive afferents are possibly the same as those involved in the acute reversal of the cortical effects of monocular deprivation that we see.

To summarize, the results reported here support previous studies which have revealed the presence of significant numbers of potentially functional inputs from the deprived eye. Furthermore our findings indicate that the outputs of both the retina and the extraocular afferents of the experienced eye must be eliminated to produce a reversal of the ocular dominance of the cortex contralateral to the deprived eye of cats monocularly deprived throughout the critical period. Lastly, we suggest that the extraocular afferents involved in this phenomenon are the proprioceptors of the extraocular muscles.

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