DEVELOPMENT OF INTEROCULAR ALIGNMENT IN CATS

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INTRODUCTION

Accurate alignment of the eyes is a necessary prerequisite for the binocular vision found in such animals as cats, monkeys and man. Stereopsis and binocular single vision demand that the subject's visual axes cross at or very near the object of regard. In cats, the tolerance for this alignment is probably less than $\pm$ 0.5° (ref. 12). The observation that every kitten at the time of normal eye-opening and throughout its first postnatal month manifests a large external deviation of its optic, and presumably visual, axes (Fig. 1) led to the present investigation of the developing interocular alignment in cats. (Interocular alignment is defined here as the angle formed by the visual axes.) In particular, this study was designed to measure the time course of, as well as factors necessary to, the development of normal interocular alignment in the cat.

MATERIALS AND METHODS

Subjects

Forty-eight cats were used in this experiment to study interocular alignment. Ten were studied as kittens, 31 as adults, and 7 periodically from birth through to adulthood. Thus the 48 cats provided data from 17 kittens and 38 adult cats.

Twenty-two of the cats were normal controls; of these 10 were studied only as kittens, 8 were studied only as adults and 4 were studied both as kittens and adults. The remaining 26 cats were studied following one of 3 experimental manipulations chosen for their known interference with binocular vision.

(1) *Six cats* had surgery designed to remove large parts of the visual cortex (at least the lateral and suprasplenial gyri and the medial half of the suprasylvian gyrus). Surgery was performed on 3 cats at 8–10 days of age, producing bilateral lesions

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in two and a unilateral lesion in the third. The other 3 were normally reared cats that had unilateral lesions as adults. For all 6, cortex was removed by gentle subpial suction under Nembutal anesthesia. The 3 infant-operated cats were studied as kittens and adults, and they are being retained for further study which to date has prevented anatomical verification of their lesions. However, observation of cortical landmarks was excellent during surgery and it is likely that the lesions are at least as large as intended. At the completion of the experiment, the adult-operated cats were sacrificed and their brains examined macroscopically. Each lesion included the intended region.

(2) *Three other cats* had their optic chiasms surgically transected by aspiration along the sagittal midline. Nembutal anesthesia and the transbuccal approach[15] were used. Attempts at rearing kittens following such surgery failed, so these 3 cats were all normally reared adults at the time of surgery. After their interocular alignments were studied, they were sacrificed, and the completeness of the chiasm sections verified by macroscopic dissection. Verification was aided by the insertion during surgery of ophthalmic gelfilm (the Upjohn Company, Kalamazoo, Mich.) into the transection between the separated optic nerve-tract pairs to prevent excessive adhesions forming between them.

(3) *The remaining 17 cats* had eyelid suture for a 6–12-month period after which the lids were parted to observe interocular alignment. The suturing was performed under ether anesthesia on 15 kittens at 8–10 days of age (5 with binocular, 9 with right-monocular and 1 with left-monocular eyelid suture) and 2 normally reared adults (one each with binocular and right-monocular eyelid suture).

Definition of terms

The following terms are commonly used in clinical studies of human interocular alignment. In adapting these terms for use with an experimental animal such as the cat it is necessary to realize that, whereas the co-operating human subject can specify his object of regard, one can never be certain of the cat's object of regard. This necessitates certain assumptions which are specified in the definitions below.

Object of regard is that object to which the alert cat visually attends at any given time.

Area centralis is that part of the cat's retina with the maximum ganglion cell density. In normal cats, objects of regard are assumed to be aligned onto the approximate center of the area centralis, making this region analogous to the human fovea.

Visual axis is the line passing through the approximate center of the area centralis and the nodal point of the eye. In normal cats, this axis is assumed to pass also through the object of regard.

Optic axis is the axis of optical symmetry of the cat's eye. While the optic axis was not properly measured in this experiment, it is probably close to the eye's axis of anatomical symmetry[21] passing near the centers of the cornea, pupil, lens, etc.

Angle alpha is the angle formed by the visual and optic axes in a given eye.

The difference between the angle formed by the two visual axes and the angle formed by the two optic axes equals the sum of the two angles alpha.

Interocular alignment is the angle formed by the two visual axes. Assuming these axes normally intersect on the object of regard for all such objects beyond a specified minimum distance from the cat's eyes, the interocular alignment may be taken as parallel for sufficiently distant objects of regard. It is further assumed that the range of the cat's binocular convergence normally matches the range of accommodation, which would set the minimum distance for convergence of the visual axes at about 25 cm from its eyes[5].

Fixation plane is the plane containing the object of regard and both nodal points of the cat's eyes.

Strabismus is an interocular misalignment causing a failure of the visual axes to intersect on the object of regard.

Divergent strabismus is a strabismus such that one visual axis (or both) lies lateral to the line joining the object of regard to the nodal point of the eye.

Convergent strabismus is a strabismus such that one visual axis (or both) lies medial to the line joining the object of regard to the nodal point of the eye.

Vertical strabismus is a strabismus such that the two visual axes are not in the same plane. It is possible for a cat to have a vertical strabismus concurrent with either a divergent or convergent strabismus.

Assessment of interocular alignments: in conscious cats

Interocular alignments of cats were assessed by two different methods. The first, a modification of a common clinical technique to detect human strabismus, was applied to every cat in this study. It required minimum restraint and no drugs. Each cat was held facing a strong light source positioned at least 4 m away. When thus viewed from the front at arm's length, each cat's eye showed a constricted pupil and reflex of the light from the cornea (Figs. 1 and 2). The reflex was aligned on the center of one pupil and the spatial relationship noted between the other reflex and pupil. With divergent strabismus this reflex is medial to the other pupil (Fig. 2b), and with convergent strabismus this relationship is reversed (Fig. 2c). The distance between pupil and reflex can be used as an approximate index of interocular alignment. (Due to the nearly vertical orientations of the constricted pupils, horizontal strabismus is much more easily discovered than is vertical strabismus; however, a sufficiently large vertical strabismus would be detected by different vertical positions of the reflexes with respect to the pupils.) Photographs such as those in Figs. 1 and 2 were taken to aid the assessment of alignments, the camera's film plane being positioned about 50 cm from the cat. With photographs, changes in pupil–reflex relationships as small as 0.5 mm were evident. Calculations based on the anatomy and optics of the cat's eye[21] indicate that each 0.5 mm separation of pupil and reflex corresponds to the eye's deviating about 7°. Kittens younger than about 3 weeks of age have cloudy corneas and poor pupillary constriction, but qualitative assessments of alignment are still possible in such kittens by this method (see Fig. 1 for example). Weather permitting,

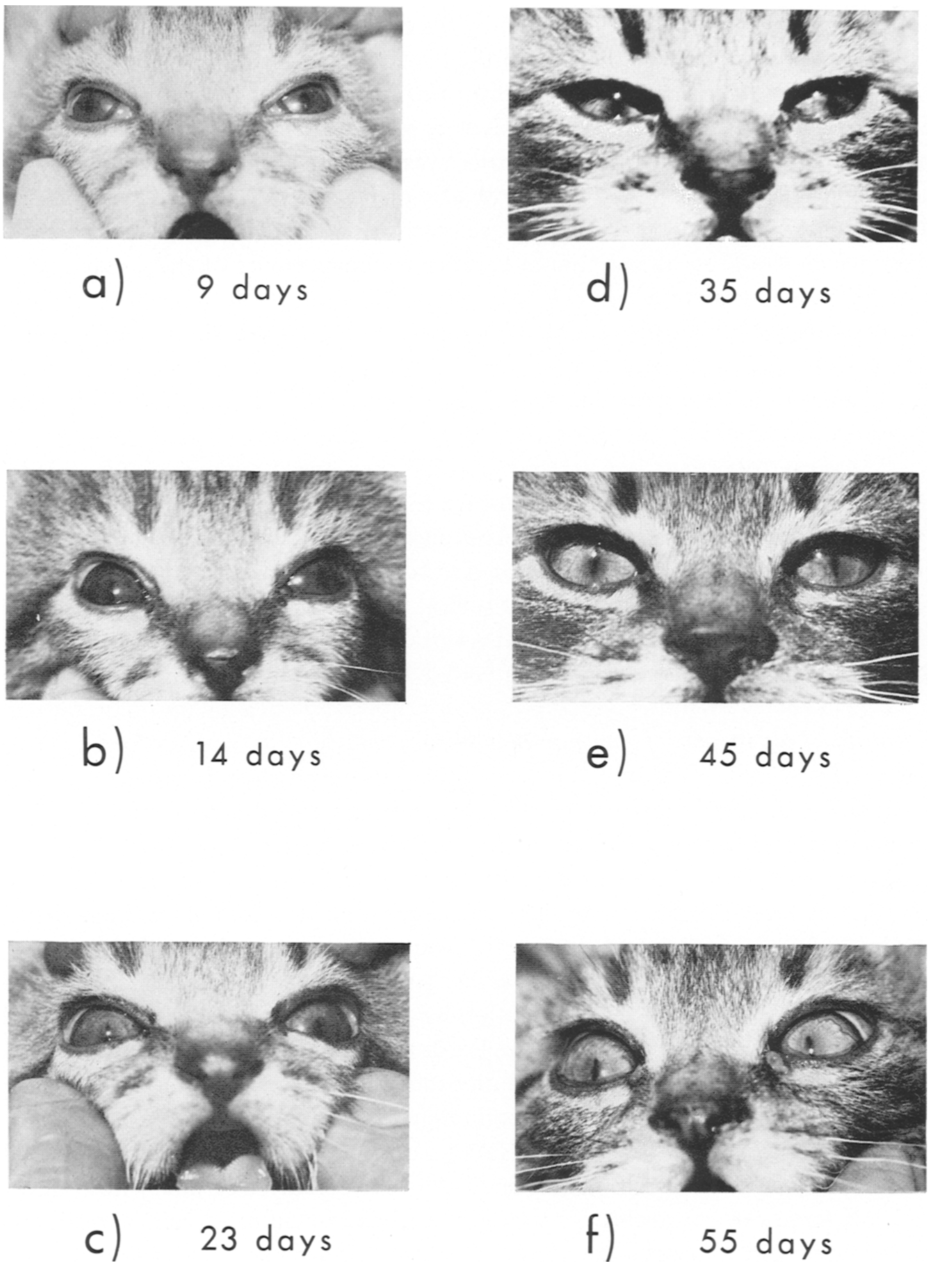

Fig. 1. Series of unretouched photographs (outdoors, sun as light source, film plane about 50 cm from subject) demonstrating the postnatal development of interocular alignment in a single kitten. a, Nine days of age. The lids were gently parted for the first time less than a minute before this photograph was taken. A large divergent strabismus is evident despite the poor pupillary constriction and cloudy appearance of the cornea. b, Fourteen days of age. A large divergent strabismus is still evident. c, Twenty-three days of age. A smaller divergent strabismus is now apparent. d, Thirty-five days of age. A still smaller divergent strabismus is shown. e, Forty-five days of age. A small divergent strabismus is still shown. f, Fifty-five days of age. No strabismus is shown. This kitten henceforth continued to show normal interocular alignment.

assessments were made outdoors (with the sun serving as the light source) as well as indoors, and interocular alignment assessments were always the same in both cases.

One assumption is basic to the application of this method: namely, that different assessments made on different cats are not due to temporarily unequal states of binocular convergence caused by the cat's visually attending to objects at various distances. The cat's maximum range of convergence, from attending to objects at infinity to those at 25 cm, is only about 8°. Since this is close to the limit for detecting changes in interocular alignment, disjunctive movements of the cat's eyes would be expected to have a minor effect on the final assessments. Two procedures were carried out to check this prediction. First, many cats were viewed while they appeared to be enthusiastically attending to small objects (pieces of meat, metal balls, etc.) moved at varying distances from their eyes. One requirement for eliciting such attention was a less intense light source for the corneal reflex markers, resulting in less pupillary constriction and consequently a less sensitive appreciation of changes in the pupil–reflex relationship. Now probably at least a 15° ocular rotation was necessary for detection. Under these conditions, good conjugate eye movements were elicited for lateral and vertical object movements, but convergent and divergent movements were never detected as the object was moved nearer to and further away from the cat's eyes. As the second check, many cats were viewed and photographed repeatedly over periods of several months and never showed detectable shifts in interocular alignment. It is therefore reasoned that any disjunctive binocular movements made by the cats during these assessments were too small to affect the final judgments of interocular alignment.

Assessment of interocular alignments: in anesthetized, paralyzed cats

By the second method, interocular alignment was assessed after anesthetizing and paralyzing the cats. Under these circumstances, the eye positions are due to the *passive* constraints of periocular tissues (especially the elasticity of the relaxed extraocular muscles[22]). The assessments are therefore a measure of these constraints which are of obvious importance for interocular alignment in the conscious animal. The technique used was part of other, terminal experiments to be communicated at a later date, and was applied to every adult cat in this study except the 3 reared with cortical lesions (thus 33 cats were studied this way).

This assessment was based on a previously described technique[1] which accurately determines the line passing through the centers of the optic disc and dilated pupil. Each cat was anesthetized with ether followed by N_2O–O_2 (70%:30%). The pupils were dilated with atropine. Eye movements were minimized by a bilateral cervical sympathectomy followed by a continuous intravenous infusion of curarizing agents[17]. The cat was placed in a stereotaxic headholder, and its head was tilted downwards by 12.5° (ref. 16). The ophthalmoscopic facilities of a specially adapted Zeiss Fundus Camera[1] were used to project the optic disc positions accurately (with an error of less than 0.1°) along a line through the center of the pupil onto a tangent screen 1 m in front of the cat. At least 3 h intervened between the onset of anesthesia paralysis and optic disc projections to allow ample time for the eyes to take up their final, stable positions. The position of the area centralis, and consequently the visual axis, can be reliably inferred (with an error of less than 2°) from a knowledge of the optic disc position[2,18,21]. Therefore, once the range of optic disc positions is established for normal cats, this method is equally sensitive to horizontal and vertical interocular misalignments caused by the passive contraints on the eyes: horizontal misalignments are seen as horizontal optic disc separations lying outside the normal range; vertical misalignments, as vertical separations outside the normal range.

Development of interocular alignment and visually guided behavior

The 14 normal kittens and the 3 kittens with cortical lesions were studied daily during their first two postnatal months to note the onset of eye-opening, interocular alignment (by the pupil-reflex method) and visually guided behavior, including visual placing and following. When held and moved towards a visible surface, a cat with visual placing extends one or both forelegs towards the surface well before tactile contact, whereas a blind cat does not. Visual following was tested by moving various stimuli (small metal balls on a rod, wads of paper on a string, etc.) in front of the animal, and a positive response consisted of its following the object with head and body. The visual testing was done in and around the home cage after temporarily removing the kitten's mother and littermates, since many kittens placed in unfamiliar environments tend to 'freeze' with fear and thus would be unlikely to respond even if capable. These visually guided responses were tested in each kitten 10–20 times daily.

RESULTS

Visual development in kittens

All 14 control kittens were born with closed eyes which spontaneously opened in the next 6–12 days. At eye-opening, all were behaviorally blind and exhibited a large divergent strabismus, these two conditions lasting until the fourth postnatal week when both began changing.

During this fourth postnatal week these kittens began making occasional (10%) positive responses to the visually guided tests (sometimes extending paws for placing, sometimes following a moving object). Improvement gradually ensued until all kittens responded positively on most (80% or more) of the tests by their seventh postnatal week. They showed no consistent trend to develop more quickly either in placing or following. These results generally agree with previous descriptions[24,27].

Development of interocular alignment followed a time course remarkably similar to that of visually guided behavior in these kittens. During the fourth postnatal week considerable fluctuations appeared in their interocular alignments: one day the eyes of a kitten appeared to have a relatively mild divergent strabismus and the next were as markedly divergent as before. The process of alignment change was never actually observed (despite many hours of observation) so it is not known whether this occurs rapidly or with slow drifts. During the next two weeks these fluctuations became less severe and less frequent. Divergence was then generally reduced in magnitude and the kittens spent more time with eyes nearly properly aligned. Typically a kitten at this age was noted for 3 days with a slight divergent strabismus, the next day with a larger one, the next two with a smaller one, etc. By the end of the seventh week fluctuations ceased, and all kittens had stable and normal interocular alignments. Fig. 1 shows the changes occurring in the interocular alignment of a typical kitten. While there was no apparent daily correlation between a kitten's visual behavior and its interocular alignment, these two features developed during the same few weeks in the kitten's life.

The 3 kittens reared with neonatal cortical ablations showed no abnormalities in their development of either visually guided behavior or interocular alignment. The lesions neither prevented nor significantly slowed these processes.

Interocular alignments during consciousness

Fig. 2a is a normal cat when viewed by the pupil-reflex method, and all 12 normals 'appeared' to have a mild divergent strabismus. This strabismus, however, is only apparent, because as Bishop *et al.*[2] have shown, the cat's optic axis projects lateral to the visual axis, so that when the visual axes are aligned parallel, the optic axes diverge. Their measurements demonstrated large variations in the angles alpha measured in 9 cats (mean = 13°; range = 5°–25°)[2]. The pupil-reflex method, in fact, assesses approximate alignment of the optic axes, from which alignment of the visual axes must be inferred. Enough control cats were therefore studied in order to establish an accurate baseline against which to compare a suspected strabismus. The criterion for strabismus is a pupil–reflex relationship falling outside the range of relationships established for the 12 control cats. This has been established as the light reflex appearing within the range bounded by 1 mm to 2 mm medial to one pupil after superimposition of the reflex on the other pupil. Previous calculations based on the optics and anatomy of the cat's eye[21] indicate that the sum of the two angles alpha for the 12 normal cats of this study varies from about 14° to 28°. Though slightly smaller, these values are in good agreement with the measurements of Bishop *et al.*[2]. Whereas this pupil-reflex method allows confident assessment of the presence and direction of a sufficiently large strabismus, the normal variation in the angles alpha renders difficult more quantitative assessments of the strabismic angles.

Fig. 2 illustrates an example of each of the assessments made by this method: (a) a normal cat (which happens to be the mother of the kitten in Fig. 1); (b) an experimental cat with a divergent strabismus; (c) an experimental cat with a convergent strabismus; and (d) an experimental cat with no apparent strabismus. Table I summarizes the results of assessing horizontal interocular alignments of all cats. By this method only one cat (R6) appeared to have a vertical strabismus (left optic axis elevated with respect to the right); unfortunately, a clear photograph of this was not obtained. Many of the cats (including one of the cats reared with binocular and two reared with right-monocular eyelid suture) were observed repeatedly over a several

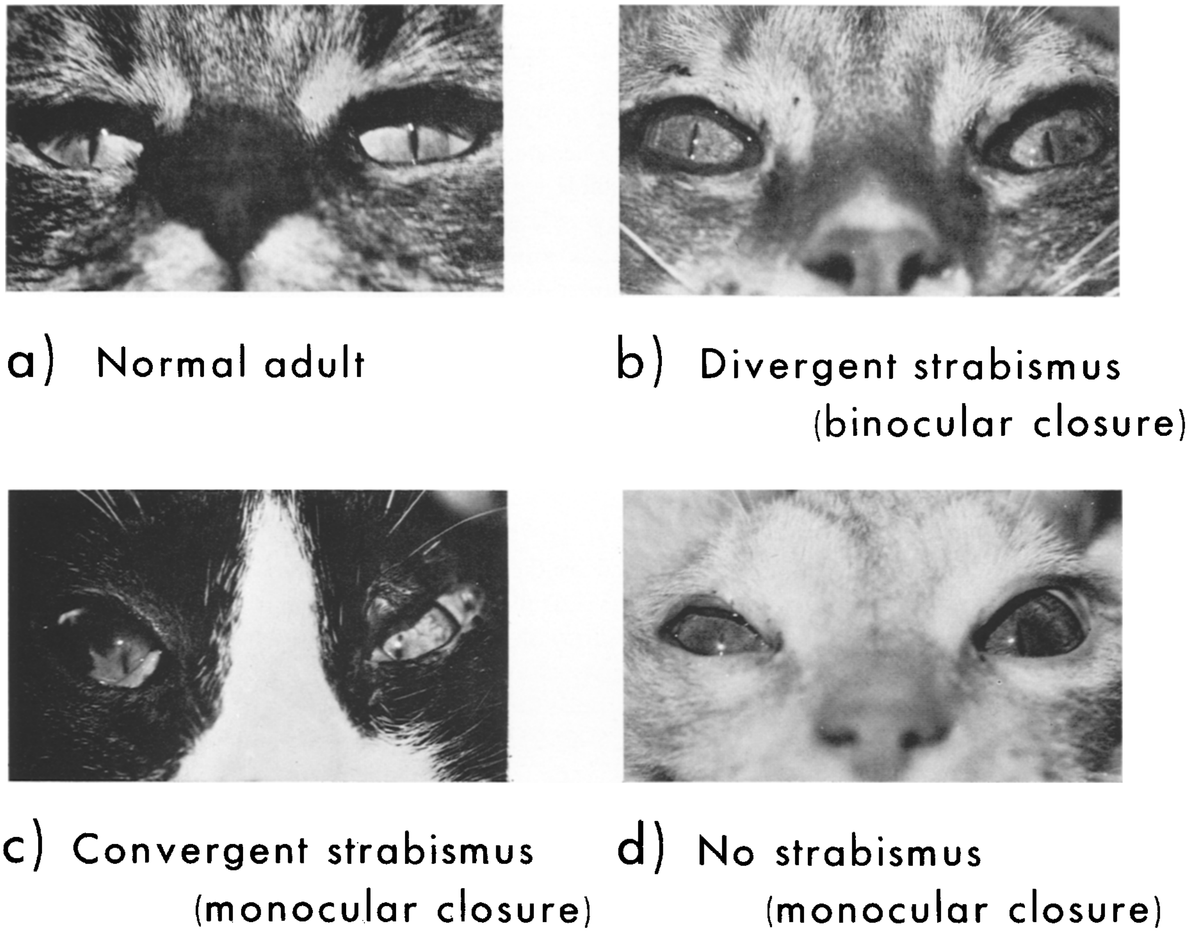

Fig. 2. Unretouched photographs (outdoors, sun as light source, film plane about 50 cm from subject) demonstrating the different interocular alignments assessed by the pupil-reflex technique. a, Control cat with no strabismus but demonstrating a divergence of its optic axes as predicted by Bishop *et al*[2]. One light reflex is superimposed on its left pupil while the other reflex falls 2 mm medial to its right pupil. In similar photographs of the other control cats, one light reflex was always found within the range 1 mm to 2 mm medial to one pupil after superimposition of the other pupil-reflex pair. b, Cat reared with binocular eyelid suture exhibiting a divergent strabismus. After superimposition of the right pupil-reflex pair, the left light reflex is found 2.5 mm medial to the left pupil. c, Cat reared with left-monocular eyelid suture (L10 of Table I) exhibiting a convergent strabismus. After superimposition of the left pupil-reflex pair, the right reflex is found slightly *lateral* to the right pupil. d, Cat reared with right-monocular eyelid suture (R9 of Table I) exhibiting no apparent strabismus. After superimposition on the right pupil-reflex pair, the left reflex falls within the 1–2 mm range medial to the left pupil.

TABLE I

ASSESSMENT OF INTEROCULAR ALIGNMENTS IN CONSCIOUS CATS

The interocular alignment of every cat in this experiment has been measured by the pupil-reflex method (see Materials and Methods), and the individual assessment for each is given in the Table. Since only the cats reared with monocular eyelid suture presented intragroup variation, only these have individual labelling in the Table (R1–R9 are those with right-monocular deprivation; L10 is the cat with left-monocular deprivation). The Table lists only horizontal strabismuses indicated by a pupil–reflex relationship outside the indicated range for normal cats. No apparent vertical strabismus was seen except for R6, whose left optic axis seemed elevated with respect to its right optic axis.

	Normal alignment (reflex 1–2 mm medial to pupil)	*Divergent strabismus (reflex >2 mm medial to pupil)*	*Convergent strabismus (reflex lateral to pupil)*
Newborn kittens*	0	14	0
Normal cats*	12	0	0
Adult visual cortex lesion	3	0	0
Reared with visual cortex lesion	3	0	0
Adult optic chiasm section	3	0	0
Adult binocular eyelid suture	1	0	0
Reared with binocular eyelid suture	0	5	0
Adult monocular eyelid suture	1	0	0
Reared with monocular eyelid suture:	2	4	4
R1	—	1	—
R2	—	—	1
R3	—	—	1
R4	1	—	—
R5	—	1	—
R6	—	1	—
R7	—	—	1
R8	—	1	—
R9	1	—	—
L10	—	—	1

* Four of these 22 cats were the same individuals.

month period but never demonstrated measurable fluctuations in interocular alignment.

Three major points emerge from Table I and are summarized graphically in Fig. 3.

(1) As already noted, all cats are born with a large divergent strabismus which they normally correct during postnatal development (Fig. 1).

(2) Rearing with deprivation by eyelid suture generally resulted in strabismus (Fig. 2b and c), whereas none of the other experimental manipulations produced a measurable strabismus. Rearing with either monocular or binocular deprivation led to strabismus ($P < 0.001$ on a χ^2 test for either compared to the normal cats).

(3) Early monocular deprivation created a more variable strabismus than did early binocular deprivation ($P < 0.001$ on a *variance ratio* test).

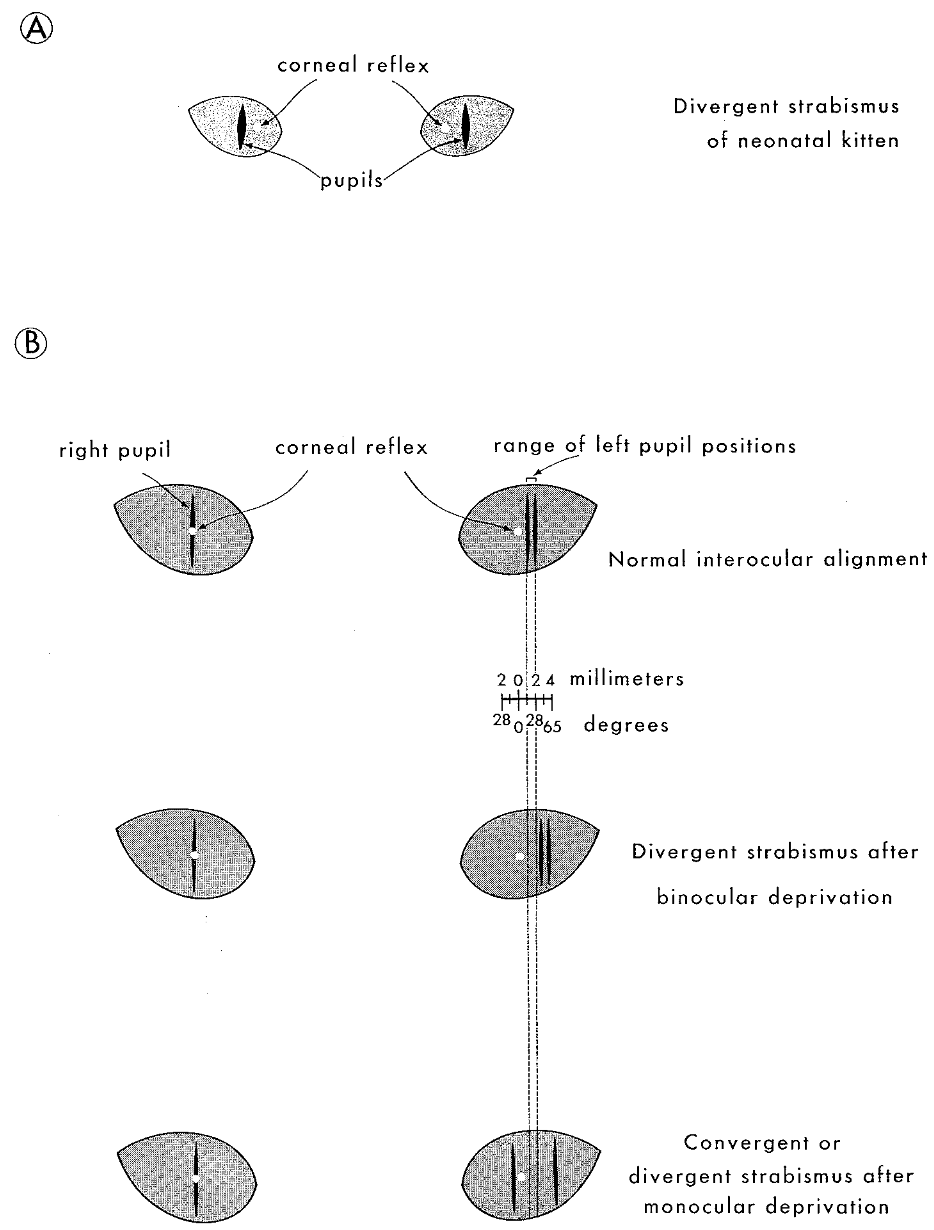

Fig. 3. Graphic summary and reconstruction to approximate scale of interocular alignment assessments made by the pupil-reflex technique. A, Neonate kitten showing a large divergent strabismus. B, Different assessments made in 3 representative groups of adult cats. The corneal reflex is shown superimposed on the right pupils, and the range of pupil–reflex relationships is seen in the left eyes. Due to the structure of the cat's eye[21], rotations of the eye result in apparent movements of the pupil while the corneal reflex remains nearly stationary. In *normal cats* the left pupil falls 1–2 mm lateral to the left reflex; in *cats reared with binocular eyelid closure* the left pupil falls 2.5–3.5 mm lateral to the left reflex; and in *cats reared with monocular eyelid closure* the left pupil falls from 1 mm medial to 4 mm lateral to the left reflex. Since this technique probably measures alignment of the optic axes (from which true interocular alignment must be inferred), the scale for the left eyes indicates the approximate divergence of these axes. Normal cats showed about 14–28° divergence of the optic axes, which is in good agreement with the data of Bishop *et al.*[2].

Interocular alignments following anesthesia and paralysis

Thirty-five of the adult cats had their interocular alignments assessed following anesthesia and paralysis. The optic disc projections served as indices of the visual axes (see Materials and Methods). *It is stressed that these assessments are made on paralyzed eyes and thus reflect passive periocular tensions.* In the normally paralyzed cat, each optic disc projects lateral to and above the middle of the fixation plane due to a combination of the following factors: the optic disc lies medial to and below the area centralis on the retina, paralysis causes divergence of the eyes, and the eyes are, of course, horizontally separated.

For the 12 normal cats, horizontal and vertical separations of the optic disc projection pairs were measured at the 1 m tangent screen, and the *mean* and *standard deviation* calculated for each. These values, which have been reconstructed in Fig. 4, are in good agreement with earlier measurements[2,16,18]. An interocular misalignment is distinguished by a separation of the optic disc projections lying outside two *standard deviations* of the *means* in normal cats. Both horizontal and vertical separations were considered in evaluating possible misalignments. By this criterion, the 3 cats with adult visual cortex lesions, the 3 cats with adult optic chiasm sections, and the 2 cats with adult eyelid suture all had normal interocular alignments after anesthesia and paralysis.

The interocular alignments of the cats reared with deprivation, however, were quite abnormal. This is presented graphically in Fig. 4A which shows the region representing the criterion of normal interocular alignment and the horizontal and vertical optic disc separations of the animals reared with eyelid suture. Separations are compared after first arbitrarily superimposing the left optic discs. With the exception of R9, each of these cats displayed an abnormal optic disc separation. If the cats are grouped into the 12 normals, 5 reared with binocular eyelid suture and 10 reared with monocular eyelid suture, significant intergroup differences are seen. The binocularly deprived cats had larger optic disc separations than the normals ($P < 0.001$ on a t-test). The monocularly deprived cats differed by virtue of the greater variability of their optic disc separations (whether horizontal or vertical separations are considered) than either the normals or the binocularly deprived cats ($P < 0.001$ on a *variance ratio* test). Thus while all of the binocularly deprived cats displayed a divergent interocular alignment, some of those monocularly deprived showed a divergent misalignment (R1, R5, R6, R8), some showed a convergent misalignment (R2, R3, R7, L10), some showed a vertical misalignment (R4, R6, R8) and R9 showed a normal interocular alignment.

Another feature noted in the optic disc projections of cats reared with eyelid suture was that both eyes, even in the monocularly deprived, had approximately equal disturbances in alignment. Fig. 4B shows a reconstruction of the optic disc projections for each eye of the cats reared with eyelid suture as well as the region to which the left and right optic discs projected in the 12 normal cats. It is perhaps not surprising that each eye of the 5 binocularly sutured cats was slightly divergent to account for the data in Fig. 4A. However, the non-deprived eyes of the monocularly

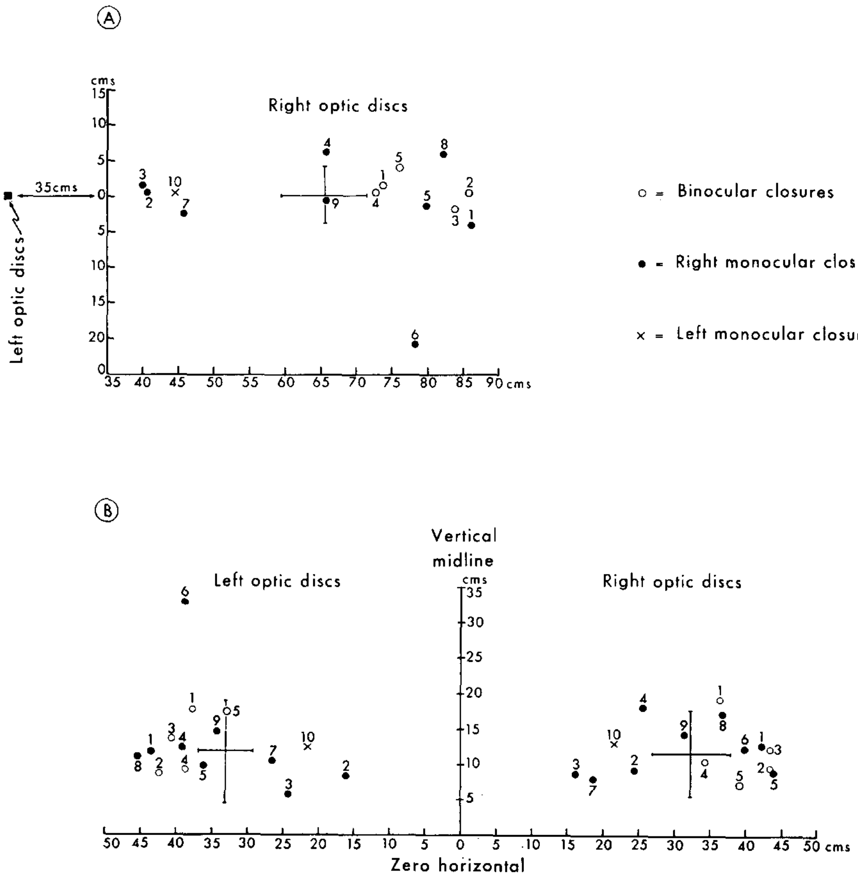

Fig. 4. Assessments of interocular alignments by optic disc projections in anesthetized, paralyzed cats. A, Individual optic disc separations for cats reared with eyelid suture compared to the normal range for the 12 control cats. For all cats, the left optic discs are arbitrarily superimposed and the separation noted by the position of the right optic disc relative to that of the left optic disc. The separations for the normal cats are indicated by a cross. Each of the 4 arms of the cross represents two *standard deviations*; and these arms meet at the *mean*. Individual optic disc separations are labelled only for those reared with eyelid suture. The symbol ○ (1–5) indicates those reared with binocular eyelid suture; ● (1–9) indicates those reared with right-monocular eyelid suture (R1–R9 in Table I); and × (10) indicates the cat reared with left-monocular eyelid suture (L10 in Table I). B, Reconstruction of optic disc projections for each eye of the cats reared with eyelid suture. Each optic disc position is labelled individually as in (A), and the left and right optic disc of each pair is indicated. The vertical midline represents the intersection of the tangent screen with the plane through the cat's sagittal midline. The zero horizontal is an arbitrary line drawn at the same place on the tangent screen for each cat, and is calculated from the data of Nikara *et al.*[16] to be the intersection between the tangent screen and fixation plane. Both of the crosses on the left and right represent the optic disc projections for the normal cats, as in A.

deprived cats were, on the whole, as equally misaligned as were the deprived eyes, and always in the same horizontal direction. In fact, there is a significant, positive correlation ($r = +0.753$, $P < 0.01$) between the paired optic disc positions for each of the 10 cats reared with monocular deprivation.

DISCUSSION

The normal interocular alignment seen in adult cats is clearly something which they acquire after birth. Their neonatally divergent eyes gradually take up positions of normal interocular alignment during the second postnatal month, at the same time as they develop visually guided behavior This month is also crucial to other aspects of feline visual development: (1) *physiologically*, this is a 'critical' period in the formation of visual connections in the brain[11]; and (2) *anatomically*, the kitten retina and lateral geniculate nucleus complete much of their development[4,13]. The same visual deprivation which interferes with interocular alignment also causes changes in the anatomy[11,13] and physiology[8,11,25,26] of the feline visual system, as well as in the animal's visual behavior[3,7]. Therefore, the kitten's development of interocular alignment seems closely linked to its development of behavior, physiology and neuroanatomy: all mature during the same period and all are disturbed by early visual deprivation.

Certain comparisons can be made between the data of this study and clinical knowledge of human interocular alignment. Humans often develop strabismus following early blindness[6,19]. Also, human neonates, like kittens, lack the normal adult interocular alignment. However, unlike the consistent divergent strabismus apparent in kittens, the human misalignment is characterized by eyes which 'move independently and irregularly until 5 or 6 weeks after birth when the movements become truly coordinated (conjugate)'[23]. These independent and irregular movements may be homologous to the spontaneous interocular alignment shifts described for neonate kittens. The major difference between humans and kittens regarding their development of interocular alignment may be their postnatal starting points: kittens are born with a divergent strabismus whereas human neonates demonstrate no consistent strabismus. While such comparisons between humans and cats must be treated with obvious caution due to large differences between the human and feline visual systems, it may nevertheless be useful to consider the mechanisms for human interocular alignment in the light of certain conclusions drawn from this work.

Whereas the development of interocular alignment in the cat seems to require a binocular visual input, once achieved in the normally reared cat, normal alignment is unchanged by a large variety of manipulations which interfere with binocular vision. When performed on normally reared adult cats, neither visual deprivation, optic chiasm sections nor unilateral visual cortex lesions result in strabismus. Furthermore, although it requires a binocular visual input, interocular alignment apparently can develop without the visual cortex, since kittens reared with visual cortex ablations showed normal development of interocular alignment. Further work is necessary to define the neural substrate responsible for this development.

The consistent finding of this study is that cats with early visual deprivation have strabismus. This was not reported in previous deprivation studies[3,7,8,11,25,26], but feline strabismus is difficult to detect for several reasons. In the conscious cat, strabismus would be effectively masked by the normally dilated pupils and the angle between the visual and optic axes. One could easily ignore the strabismuses demonstrated in Fig. 2b and c, if these factors were not carefully controlled. For a clear demonstration of an interocular misalignment in anesthetized, paralyzed cats, a preparation is required which minimizes eye movements and variations in the final eye positions; a larger scatter in optic disc projections in the normal cats than that reported here would make such assessments unclear. The preparation evolved for this study[17] effectively minimizes these problems so as to allow clear determinations of interocular misalignment.

The interocular misalignments caused by early visual deprivation were apparent both while the cats were fully conscious (thus representing strabismus) and after they were anesthetized and paralyzed (thus representing abnormal passive tensions in the periocular tissues). A comparison of Table I and Fig. 4 shows that, for each cat, assessments of horizontal interocular misalignment were in agreement for both states (consciousness and anesthesia paralysis). The agreement for vertical misalignment is admittedly weaker (the one case of a vertical strabismus in R6 with an elevated left visual axis agrees with the plots reconstructed in Fig. 4), but this is to be expected due to the relative insensitivity of the pupil-reflex method for vertical, as opposed to horizontal, strabismus. Assessments by both methods provide the same conclusions that none of the manipulations performed on adults affected their interocular alignment, that early deprivation causes strabismus, and that the early monocular deprivation causes more variable strabismus than does the early binocular deprivation.

This agreement is emphasized by way of evaluating an important result derived solely from assessments in anesthetized and paralyzed cats, namely that *both* eyes of the cats reared with monocular eyelid suture were symmetrically misdirected. (It was not possible to determine the individual contributions of each eye to the overall strabismus by means of the pupil-reflex method as used in this experiment.) However, two tentative conclusions are drawn from these data: (1) the misalignments are not due to a simple mechanical effect of suturing the lids, and (2) early monocular deprivation interferes with interocular alignment not by misdirecting the deprived eye, but rather by causing an inappropriate balance of muscular tensions to develop symmetrically in the two eyes. Certain inferences are drawn from these results, and a working hypothesis is put forward to explain some aspects of the developing interocular alignment of kittens. If this development is under visual control, as indicated by the results of early visual deprivation, then the visual sensory input must include cues for aligning the visual axes. This input must therefore allow the visual system to distinguish between diplopia and binocular single vision; that is, it must be a patterned and binocular input. The balance of tensions in the neonate extraocular muscles favor a large divergence of the visual axes. It is hypothesized that binocular, pattern vision during normal visual development stimulates and directs the visual system to alter these tensions thereby increasing convergence of the visual axes until normal interocular alignment is established. This new balance of tensions is permanent, and the adult cat can modify them only slightly so as to allow the small (up to about 8°) disjunctive binocular movements necessary for binocular fusion of objects of regard at different distances.

When the developing visual system has no patterned input, as in early binocular deprivation, there is no stimulus for the eyes to fixate and thus no visually directed alterations are made in the neonatal balance of extraocular muscle tensions. The final alignment is one of divergence, although apparently less so than in the neonatal animal. Perhaps the moderate amount of alignment correction seen in such cats merely reflects the normal postnatal development of the orbits and their tissues without visual influence.

On the other hand, early monocular deprivation seems to allow the feline visual system to respond normally to patterned stimuli available to the non-deprived eye as evidenced by behavioral experiments[3,7] as well as physiological recording in the striate cortex[8,11,26] and superior colliculus[25]. The monocular patterned input stimulates the developing visual system to align the non-deprived eye with various objects of regard by altering tensions in the extraocular muscles. Commands sent to the extraocular muscles normally produce coordinated movements of both eyes, but without a binocular, patterned input, the visual system has insufficient data to balance the tensions in binocularly yoked pairs of extraocular muscles. Therefore the final balance of tensions which is developed creates a wide range of interocular alignments.

As yet much of the above speculation lacks experimental support. A further important result which is lacking is a positive identification of that part of the visual system responsible for developing the normal, interocular alignment. This need not be a compact area, but may include parts of such separated structures as the superior colliculus and the visual cortex. Furthermore, the potential to balance tensions in the extraocular muscles might reside independently in several neural areas, a redundancy not uncommon to the central nervous system. At present all that can be said about this is that the cat's visual cortex seems unessential to developing interocular alignment despite its well-documented role in binocular patterned vision[1,9,10,14,20].

SUMMARY

Kittens are born with a large divergent strabismus. Fourteen kittens observed daily from birth concurrently developed both visually guided behavior and normal interocular alignment during the second postnatal month. (Interocular alignment is defined as the angle formed by the visual axes.)

Once achieved, this normal interocular alignment is resistant to a number of alterations in the cat's visual input. Two cats with adult eyelid closure (one binocular, one monocular), 3 cats with adult unilateral visual cortex ablations, and 3 cats with adult transection of the optic chiasm along the sagittal midline did not develop strabismus.

However, all 5 kittens reared with binocular eyelid closure and 9 of 10 reared with monocular eyelid closure developed a stable strabismus. The former all displayed a similar divergent strabismus whereas strabismus in the latter covered a wide range of interocular misalignments. A purely mechanical explanation is discarded since *both* eyes of cats reared with monocular closure were similarly misaligned. These results

indicate that cats require a normal, binocular visual environment during development to achieve the proper interocular alignment.

It is hypothesized that during normal development, the binocular patterned visual input stimulates some part or parts of the cat's visual system to align the eyes properly. Binocular closure results in no patterned stimulation, so the eyes remain diverged. Monocular closure allows patterned stimulation through the open eye, and this initiates alignment which results in a wide range of errors due to the lack of data from the closed eye. Apparently the visual system does not require the visual cortex for this alignment since 3 kittens reared with extensive visual cortex ablations made during the 8th postnatal day demonstrated the normal development of both visually guided behavior and interocular alignment.

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