

The spatial localization deficit in visually deprived kittens

Guy Gingras^a, Donald E. Mitchell^{a,*}, Robert F. Hess^b

^a *Department of Psychology, Dalhousie University, South Street, Halifax, N.S., Canada B3H 4J1*

^b *Vision Research Unit, Department of Ophthalmology, McGill University, Canada*

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Abstract

We measured the spatial localization abilities (alignment accuracy) of visually deprived kittens by use of similar spatially band-pass stimuli (Gaussian blobs) to those employed for the assessment of human amblyopes. The tests of vision were conducted on kittens reared with either strabismus or following different periods of monocular deprivation. As with amblyopic humans, the deficits in alignment accuracy were scaled in proportion to blob size and were not only considerably larger than those of grating acuity but also were not correlated with either the acuity or contrast sensitivity losses. Tests with stimuli of various contrast revealed that the deficits could not be explained in terms of the contrast sensitivity loss in this eye. The positional deficits that arise from anomalous visual development are independent of the contrast sensitivity loss and profound.

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1. Introduction

Attempts to define the nature of the neural deficits that underlie the complex perceptual deficits associated with human amblyopia have employed two converging approaches. The first approach, and the more direct in so far as delineating the neural deficit, has been to document the anatomical and physiological abnormalities in the visual cortex of kittens and monkeys that had been reared with certain forms of selected visual deprivation in early life in order to induce amblyopic-like visual deficits. The second approach and the more direct in so far as identifying key aspects of the perceptual deficit, has been to employ sophisticated psychophysical probes of the visual abilities of human amblyopes. Congruence between both approaches is needed for an adequate understanding of the neural basis of the per-

ceptual dysfunction that characterizes amblyopia. Until it can be shown behaviourally that animals with certain forms of selected visual deprivation in early life exhibit similar characteristic deficits to that of human amblyopes, there is little hope of understanding their neural basis and to tease apart contesting explanations for the visual deficits based on either loss (undersampling) or rearrangement (spatial scrambling) of connections within cortex (Daw, 1995; Kiorpes & McKee, 1999).

At first glance, the visual deficits that have been documented in visually deprived animals appear to be similar to those experienced by their human counterparts. For example, different forms of deprivation result in deficits, of one degree or another, for spatial resolution and contrast sensitivity as well as losses to positional accuracy in both monkeys (e.g. Harwerth, Smith, Boltz, Crawford, & von Noorden, 1983; Kiorpes, 1992; Kiorpes, Kipers, & Movshon, 1993; Kiorpes, Tang, Harken, & Movshon, 2003) and cats (e.g. Lehmkuhle, Kratz, & Sherman, 1982; Mitchell, 1988; Mitchell, Ruck, Kaye, & Kirby, 1984; Murphy & Mitchell, 1991) and man (see reviews by Daw, 1995; Hess, 2002; Levi & Carkeet,

* Corresponding author. Tel.: +1 902 494 6419; fax: +1 902 494 6585.

E-mail address: d.e.mitchell@dal.ca (D.E. Mitchell).

1993). A closer look, however reveals that there is an important unresolved issue between the animal models and the human condition regarding positional uncertainty, which is considered the defining characteristic of human amblyopia (Bedell & Flom, 1981; Demanins & Hess, 1996; Fronius & Sireteanu, 1989; Hess, Campbell, & Greenhalgh, 1978; Hess & Holliday, 1992b; Lagrèse & Sireteanu, 1991; Levi & Klein, 1992; Wilson, 1991).

Superficially, there is a close agreement between the vernier acuity deficits exhibited in animals made artificially amblyopic (Kiorpes et al., 1993; Murphy & Mitchell, 1991) and their human counterparts (Bradley & Freeman, 1985; Levi & Klein, 1985; Levi, Klein, & Yap, 1987). However, it is also known that both in animals made artificially amblyopic (Kiorpes et al., 1993) and human amblyopes (Levi & Klein, 1985; Levi et al., 1987; McKee, Levi, & Movshon, 2003), the vernier loss is strongly correlated with the contrast sensitivity loss and there is good reason to suppose that the former loss follows as a consequence of the latter (Bradley & Freeman, 1985). This is a direct consequence of vernier acuity targets having abutting features and as such are likely to involve within-filter processing (Wilson, 1991; Whitaker & MacVeigh, 1991) where performance is governed more by the detection of target spatial frequencies (Carney & Klein, 1999) or the discrimination of their orientations (Watt, 1984) than it is by the encoding of target position per se. In other words, within-filter operations rather than between-filter operations are involved. The conclusion is that such vernier-type targets are not ideal for assessing the purely positional dysfunction that many studies have shown is a characteristic feature of amblyopia (Bedell & Flom, 1981; Demanins & Hess, 1996; Fronius & Sireteanu, 1989; Hess et al., 1978; Hess & Holliday, 1992b; Lagrèse & Sireteanu, 1991; Levi & Klein, 1992; Wilson, 1991).

A more appropriate measure of positional coding necessitates the use of targets with well-separated features that require positional information derived across different cells rather than within the same cell. A number of different approaches have been adopted (Bedell & Flom, 1981; Fronius & Sireteanu, 1989; Hess & Holliday, 1992b; Levi & Klein, 1992; Weiss, Rentschler, & Caelli, 1985) all of which show that there are profound positional losses in human (mainly strabismic) amblyopes. In one such study, Hess and Holliday (1992a) used well-separated, spatially narrow-band stimuli (Gabor patches) that prevented the use of the local spatial contrast cues for spatial localization present in conventional vernier targets (Whitaker & MacVeigh, 1991). They showed that positional accuracy for such a stimulus, unlike its vernier counterpart (Bradley & Freeman, 1985), did not depend on the spatial frequency, orientation, or to a large extent, contrast of the stimuli. In a subsequent study they used this stimulus to examine

the relationship between the contrast sensitivity and spatial localization deficits in human amblyopes. The stimuli they employed also maximized the possibility that detection and localization of the stimuli were mediated by the same spatial mechanisms and, as a consequence, the data allowed for a more complete description of the spatial localization deficit than that obtained from use of conventional spatially broadband stimuli. Two key findings to emerge from this study was that the positional deficit in human amblyopes affected all spatial scales equally (i.e. the deficit was scale invariant) and was also unrelated to the contrast sensitivity loss. Thus, unlike the conclusion with vernier stimuli, human amblyopes exhibit independent positional and contrast sensitivity losses, the former being the main distinguishing feature of the human condition. The unanswered question now is, *do animals with certain forms of selected visual deprivation in early life also exhibit large and independent losses to positional coding that are both spatial scale invariant and unrelated to the loss of contrast sensitivity?*

The answer to this question will define the adequacy of our present animal models of amblyopia. If animals made artificially amblyopic exhibit similar positional deficits then we are in a position to pursue the neural substrate of what is considered to be the defining characteristic of the human condition. Furthermore, such a finding in animals also suggests an important role for experience-dependant neural development in human positional coding, an issue on which the only information available at present is derived from conventional vernier acuity studies (Shimojo, Birch, Gwiazda, & Held, 1984; Shimojo & Held, 1987).

2. Methods

2.1. Animals

The experiments were conducted on one normal cat (N1) and 8 visually deprived cats that were born and raised in a closed laboratory colony. Data was also obtained from a cat on which an attempt to induce a strabismus by surgery at 3 weeks of age was unsuccessful. This cat (N2) was tested binocularly and was classed as normal on the reasonable assumption that the non-operated eye was not impaired. The specific times of deprivation of the 8 visually deprived cats are provided in Table 1. Three of the deprived animals were monocularly deprived from about the time of natural eye opening for an extended period of time and were designated as long-term monocularly deprived (LMD1, LMD2, and LMD3). The rearing condition of LMD2 matched very closely that of an animal (60B) from which electrophysiological recordings from area 17 were made in a previously published study from this laboratory (Mitch-

Table 1

Rearing history of the experimental animals, the grating acuity of the deprived eye and the size of the deficit expressed in octaves with respect to the mean acuity of the non-deprived or non-deviating eye

Animal	Manipulation	From (days of age)	To (days of age)	Acuity in deprived eye (cycles/deg.)	Deficit (Octaves)
LMD1	MD	37	67	5.87	0.52
LMD2	MD	11	60	5.03	0.74
LMD3	MD	11	82	4.15	1.02
SMD1	MD	35	41	5.24	0.68
SMD2	MD	60	66	5.24	0.68
SMD3	MD	90	96	7.53	0.16
S1	ESO	17	—	4.82	0.80
S2	ESO	29	—	3.18	1.40

Abbreviations: MD—monocular deprivation; ESO—surgically induced esotropia.

ell, Cynader, & Movshon, 1977a). Ocular dominance histograms recorded after a period of recovery that was of sufficient length to permit asymptotic recovery of grating acuity and published in that paper indicate that only 19% of 75 cells were dominated by the deprived eye. LMD3 was deprived even longer (to 82 days of age) and so might be expected to have experienced an even greater loss of connections in area 17 with the deprived eye. A further three animals were designated as short-term monocularly deprived and received a 6 day period of MD at either 35, 56 or 90 days of age (respectively, SMD1, SMD2, and SMD3). One of the latter animals, SMD2 that received 6 days of MD at 56 days of age, was reared in total darkness until 4 weeks of age. The wide variety of different conditions of monocular deprivation were employed in the hope that the range of observed deficits of spatial localization would overlap in severity with those reported among human amblyopes (Demanins & Hess, 1996; Hess & Holliday, 1992b). Finally, two animals were reared with a surgically induced esotropia (S1 and S2). As well as describing the nature and timing of the manipulations conducted on the experimental animals, Table 1 also lists the grating acuity that was attained by the deprived or deviated eye as well as the deficits in the acuity of this eye (expressed in octaves) with respect to the mean acuity of the fellow non-deprived or non-deviated eyes.

2.2. Surgical procedures

All procedures associated with the experiments followed animal protocols approved by Dalhousie University and were in accordance with standards and regulations established by the Canadian Council on Animal Care. Six kittens were monocularly deprived by eyelid suture while the remaining two were rendered strabismic by partial myectomy of one of the extraocular muscles of one eye. The surgical procedures for both experimental manipulations were performed under gaseous halothane anesthesia following partial induction with Xylazine (*im* 2 mg/kg). A few drops of a local anaesthetic (Marcaine 0.25%) were dropped onto the

wounded tissue during the surgical manipulations and afterwards the animals received an analgesic (Butorphanol 0.4 mg/kg) in order to minimize any pain and discomfort. The simple surgical manipulation required to open the sutured eyelids at the end of the period of monocular deprivation was performed with anesthesia induced and maintained with gaseous halothane. The procedures employed for eyelid suture were identical to those described by Murphy and Mitchell (1987) who introduced two noteworthy refinements to methods employed earlier in order to increase the likelihood of a patent palpebral opening after termination of the deprivation. The first modification to the conventional procedure was to wound the eyelid margins in a different manner and the second was to introduce an additional occlusion layer. As an alternative to trimming the eyelid margins through their entire extent from just temporal to the puncta, the palpebral conjunctiva immediately adjacent to the lid margins was dissected free to expose about 3 mm of eyelid tissue. The freed palpebral conjunctiva from the lid margins were sutured together with 5-O chromic gut to form the first of two occlusion layers. Following this, the exposed tissue on the underside of the upper and lower eyelid were wounded lightly with the sharp end of a 26 gauge syringe needle, opposed together and sutured with 4-O braided silk suture thread. Because the new occlusion procedure maintained the eyelid margins, the kittens were able to keep their eyelids fully open after termination of the period of eyelid suture.

Strabismus (esotropia) was induced surgically in two kittens (S1 and S2) by removal of part of the body of the lateral rectus muscle of one eye by use of standard procedures described in detail in a previous publication (Mitchell et al., 1984). In addition to partial myectomy of the lateral rectus muscle the procedure also included removal of the nictitating membrane from this eye. The esotropia induced in these two animals was evident immediately and remains obvious to this day.

One animal that was monocularly deprived for just 6 days at 5 weeks of age (SMD1) developed an obvious esotropia several weeks after vision was restored to the

deprived eye (see Fig. 11). With the exception of LMD3 which also became esotropic but not until after 6 months of age, all the other monocularly deprived animals appeared orthotropic following termination of the period of deprivation.

2.3. Behavioural testing of visual acuity

Measurements of the visual acuity for square-wave gratings were made on a jumping stand (Mitchell et al., 1977a; Mitchell, Giffin, & Timney, 1977b) by use of procedures that differed in only one respect from those described in detail in the past (Mitchell, 1991; Murphy & Mitchell, 1987), namely the use of a discrimination rather than a detection task where the kitten was required to jump toward a vertical grating (the positive stimulus) as opposed to an adjacent horizontal grating of the same spatial frequency. The change to a discrimination task was made in order to both reduce the potential for aliasing (Hall & Mitchell, 1991; Lennie, Trevarthen, VanEssen, & Wassle, 1989; Wandell, 1995) that is possible with detection tasks and to ease the ability to achieve a luminance match of the stimuli. The stimuli (19 × 19 cm) were produced photographically (Murphy & Mitchell, 1987) and mounted on thick cardboard with a border 3.8 cm wide. The gratings had a contrast close to 1.0 and a mean luminance of 55 cd/m².

A brief description of the way in which acuity was assessed is provided here as it served as the model for the procedure used later to assess alignment accuracy. Kittens were trained to jump towards the positive stimulus (a vertical grating) that was placed adjacent to the negative stimulus on the jumping stand. The positions of the two stimuli were interchanged from left to right in a pseudo-random order (Mitchell et al., 1977a, 1977b), with correct jumps rewarded with food (pureed chicken liver mixed with regular cat food) and petting. Incorrect jumps resulted in denial of the rewards and immediate replacement of the kitten on the jumping platform so as to repeat the trial. Acuity was determined each session by use of a descending method of limits that began with assessment of the animal's performance with gratings having a spatial frequency at least 3 octaves above threshold. A key feature of the procedure was to reduce the period of the grating in very small but equal steps (equated on a logarithmic scale with as many as 12 to an octave) between successive blocks of trials. The animal received only one trial at low spatial frequencies unless an error was made in which case it received additional trials in order to establish whether it could attain a criterion level of performance that was defined as either 5 consecutively correct responses or else a minimum of 7 correct in a maximum of 10 trials. Within two octaves of the estimated threshold the minimum number of trials was increased to first 2 and then to 3 about an octave from threshold. A minimum of 5 trials

were required for the 4 highest spatial frequencies. The session was usually terminated once the animal could no longer achieve criterion performance within the maximum number of trials (10) provided at any spatial frequency. Because performance declined rapidly from flawless to chance within two incremental steps, equivalent to less than 1/6 of an octave, the threshold could be titrated quite precisely on any given session (see Murphy & Mitchell, 1987, Fig. 1). A conservative criterion was adopted for threshold, namely the highest spatial frequency for which criterion performance was met, a value for which the animal's performance could be at best flawless and at worst 70% correct. Tests of the vision of the deprived (or deviating eye) were made with the other eye occluded by an opaque hard contact lens having a base curve chosen to match as closely as possible the average corneal curvature for kittens of that age (Freeman, 1980). A drop of local ophthalmic anesthetic (proparacaine hydrochloride 0.5%) was placed into the conjunctival sac prior to insertion of the lens in order to eliminate any potential discomfort. Measurements of the vision with both eyes open were made from time to time in order to measure the acuity of the non-deprived eye as comparison measurements indicated that these measures were identical to monocular measurements made with the deprived eye occluded. Measurements of spatial localization of the monocularly deprived animals were begun 4 to 6 weeks after the visual acuity of the deprived eye had stabilized. For the strabismic animals, measurements were begun at 5 months of age, about a month after visual acuity reaches adult values (Giffin & Mitchell, 1978; Mitchell, Giffin, Wilkinson, Anderson, & Smith, 1976).

2.4. Measurement of spatial localization

The stimuli for these measurements consisted of two sets of three circularly symmetric Gaussian patches that were presented on the display screen of a computer monitor. For one set, the 3 patches were in vertical alignment, while in the other set (representing the positive stimulus for the two-choice discrimination) the middle patch was horizontally displaced from a hypothetical line joining the centers of the two vertically aligned outer patches (see Fig. 1(A)). Five sets of Gaussian blob sizes were employed with each set differing from the next by a factor of two. An example of 3 such stimuli are shown in Fig. 1(B). In Fig. 1(C) and (D), a spatially filtered (smoothed low-pass filter) version of the four smallest stimuli are shown, whose cut off was matched either to the resolution of a normal adult cat (i.e. 10c/d) or to that of our most amblyopic cat (i.e. S2 whose grating acuity deficit was 1.4 octaves). Each blob was separated by a constant 5 standard deviations from its nearest neighbor so that the displays were scaled versions of each other. Because of limitations dictated by the dimensions of

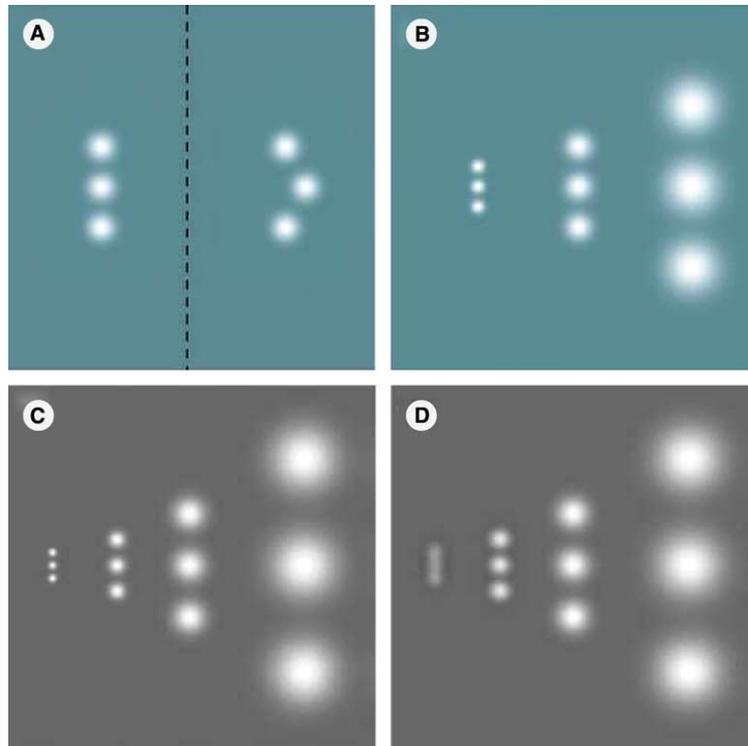


Fig. 1. (A) Illustration of the stimulus display for the tests of alignment accuracy. The kittens were rewarded for jumping toward the misaligned set of Gaussian blobs on the right as opposed to the aligned set on the left. (B) Three scaled versions of the stimuli. (C) A filtered version of the four smallest stimuli to illustrate as they would appear to a normal adult cat (i.e. an acuity of 10 c/d). (D) A filtered version of the same stimuli as (C) to illustrate as they would appear to the amblyopic eye of the most severely amblyopic (strabismic) cat investigated here (S1 had an acuity deficit of 1.4 octaves).

the monitor screen, the largest stimulus set could not be displayed on the screen at the same observation distance as was used for the other displays; instead the animals were tested with the fourth largest set at half the observation distance (30 versus 60 cm) thereby maintaining the scaled relationship between stimulus sets. Gaussian stimuli were used in this study rather than Gabors as employed by Hess and Holliday (1992a) in order to increase their visibility. Moreover, because Hess and Holliday (1992a) showed that spatial localization for the latter stimulus did not vary with either the spatial frequency or orientation of the carrier frequency, data obtained with Gaussian targets should be identical to that obtained with Gabors.

Because of constraints dictated by the size of the monitor screens and the minimum observation distance that could be employed for jumping, the separation of the Gaussian blobs was smaller (5 versus 10 standard deviations) than that employed by Hess and Holliday (1992a, 1992b) for their studies on humans. For most of the measurements reported here the stimuli were displayed on a NEC Multisync monitor (Model JC-1401P3A) monitor. The luminance and contrast of the stimuli and calibration of the monitor were made by use of a United Detector Technology Model 161 Optometer. The background luminance was 0.5 cd/m^2 .

The animals were trained initially to jump towards the stimuli with a large misalignment of 4 cm. This simple task was usually learned in the first session. On subsequent sessions the offset was reduced in small steps that were equated on a logarithmic scale (8–10 steps to the octave within an octave of threshold) until the cat could no longer achieve criterion performance. Criterion performance was defined as it was for the measurements of grating acuity, namely at least 7 correct out of a maximum of 10 trials for any given offset. Performance was usually flawless with all offsets other than smallest ones close to threshold. A conservative criterion was employed to define the threshold offset on any given testing session, namely the smallest offset for which performance was 70% correct or better. Separate measurements were made on several animals with both left and right offsets but as the results appeared identical most data was collected with just left offsets. The performance of the non-deprived eye was assessed on the basis of binocular measurements as the performance on the latter was shown in control experiments to be identical to the monocular performance of the non-deprived eye. Moreover, because binocular measurements could be made without the use of a contact lens occluder, they could be followed immediately by measurements of the alignment accuracy of the deprived eye made with the

fellow eye occluded thereby permitting comparison of the performance of the two eyes in a single daily session. The thresholds reported for each stimulus condition represent the mean of at least 3 measurements. In the vast majority of cases these thresholds were sufficiently similar that the standard errors were extremely small and always less than the size of the symbols that depict the data in each of the figures that follow.

3. Results

3.1. Spatial localization—normal animals

The dependence of alignment accuracy on the size of the Gaussian blobs (expressed in terms of their standard deviation) is illustrated in Fig. 2 for the two normal cats tested binocularly. There was a proportional relationship between the two variables indicating that, like humans (Hess & Holliday, 1992a, 1992b; Toet & Koenderink, 1988; Toet, von Eekhout, Simons, & Koenderink, 1987), alignment accuracy scaled with blob size.

3.2. Spatial localization—monocularly deprived animals

The alignment accuracy of the deprived and non-deprived eye of the three long-term monocularly deprived animals are displayed in Fig. 3 as a function of blob size. Despite their high contrast (0.685), measurements of alignment accuracy could not be made with the deprived eye for the two smallest blob sizes nor was it possible to obtain data with the largest stimuli because of the limits on the maximum displacement set by the dimensions of the display screen of the monitor. The data for the non-deprived eye of these animals followed a very similar pattern to that observed in the two normal cats with alignment accuracy scaling with blob size. Although alignment accuracy with the deprived eye was considerably worse (by a factor of 8–13) than that of the non-de-

prived eye, the data for the two blob sizes for which measurements with the deprived eye were possible suggest that alignment accuracy scaled with blob size for this eye as well.

Data on the alignment accuracy of the three animals deprived for just 6 days are displayed in Fig. 4. Measurements with the deprived eye were possible with only one blob size for SMD1, three for SMD2 and four for SMD3. Although alignment accuracy was poorer with the deprived than the non-deprived eye for all three animals, the interocular difference was greatest for SMD1 and smallest for SMD2. The fact that the deficit was largest in the animal that was deprived earliest was not a surprise as the 6 day period of MD was initiated at the height of the sensitive period in area 17 (Olson & Freeman, 1980). However, the pattern of results in the other two animals was somewhat unexpected as the monotonic decline in cortical plasticity past 5 weeks of age would suggest that the deficits should be smallest in the animal deprived last (SMD3). Another interesting and unexpected observation is made evident in Fig. 5 which shows the ratio of the alignment accuracy between the two eyes for each animal. For those animals (all but SMD1) for which measurements of alignment accuracy were possible for more than one blob size with the deprived eye, the ratio plotted in Fig. 5 was the mean of the ratios calculated for each blob size for which measurements were made with both eyes. Interestingly, the ratios for two of the three short-term MD animals either equaled (SMD3) or exceeded (SMD1) the ratios for the long-term MD group. For only one of the former animals (SMD2) was the ratio smaller than that observed among the latter group.

3.3. Spatial localization—strabismic animals

The alignment accuracy of the two eyes of the strabismic cats are plotted in Fig. 6. As with the non-deprived eye of the monocularly deprived animals, the alignment accuracy of the non-deviating eye of S1 and S2 scaled

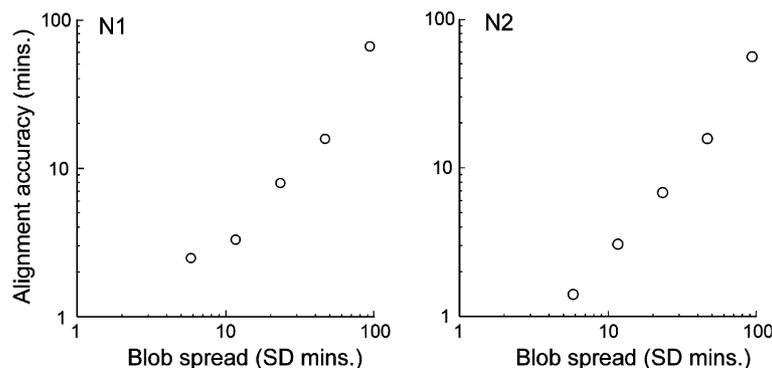


Fig. 2. Alignment accuracy in min of arc of the two normal cats (N1 and N2) as a function of the spatial scale of the Gaussian blobs expressed in terms of their standard deviation (SD in min of arc). The stimuli all had the same high contrast of 0.685.

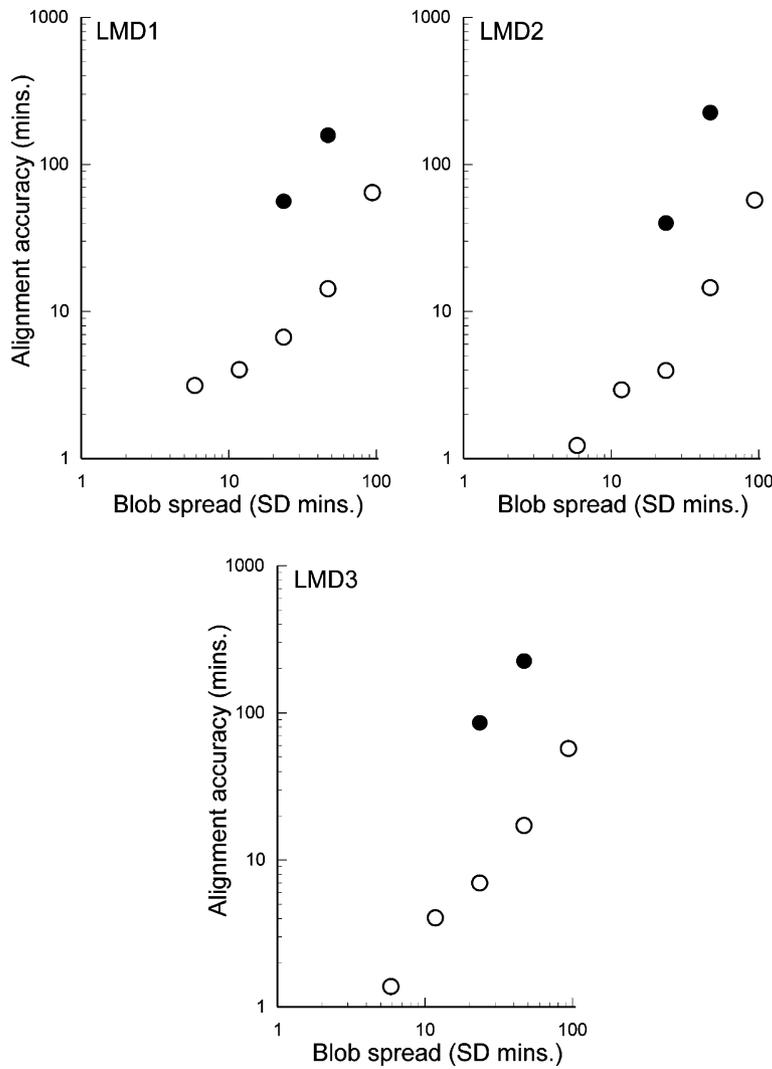


Fig. 3. Alignment accuracy in min of arc of the two eyes of the three long-term monocularly deprived cats (LMD1, LMD2, LMD3) as a function of the spatial scale of the Gaussian blobs (blob size) expressed in terms of their standard deviation (SD in min of arc). The stimuli all had the same high contrast of 0.685. Open and closed symbols depict the performance of respectively, the non-deprived and deprived eye. Measurements were possible for only two blob sizes with the deprived eye.

with blob size. For both strabismic animals, measurements of alignment accuracy with the deviating eye were possible for only the mid blob size. And as illustrated in Fig. 5, the ratio of the alignment accuracy of the two eyes measured for this blob size was greater than that observed in any of the monocularly deprived animals.

The fact that, like amblyopic humans, performance with both eyes of the experimental animals scaled with blob size was reassuring despite the use of a smaller blob separation (5SD) than that employed by Hess and Holliday (1992b) on humans (10SD). In fact, pilot data obtained from the non-deprived eyes of four animals with blobs having an SD of 11.46 min (Fig. 7) indicated that the separation employed here was within the range for which alignment accuracy varied little with element separation. Overall, the effect of element separation was similar to that reported for humans with stimuli imaged in the fovea (Hess & Hayes, 1994).

3.4. Effects of contrast on alignment accuracy

A series of measurements were made in order to explore the possibility that the deficits observed in the deprived or deviating eye of the experimental animals could be attributed to the lower effective contrast of the stimuli as seen by this eye. It might be thought that this would be unlikely since the stimuli were presented at very high physical contrast (0.685). However, since measurements of the dependence of alignment accuracy of Gaussian blobs on contrast have not been made previously for the cat, the possible contribution of a contrast deficit to the alignment accuracy of the deprived or deviating eye was explored for the mid-size blobs (SD 22.9 min) in one normal and four experimental cats (3 MD and one strabismic cat). Because stimuli of a given physical contrast may appear very different with the two eyes, a rigorous test of the idea that the contrast loss

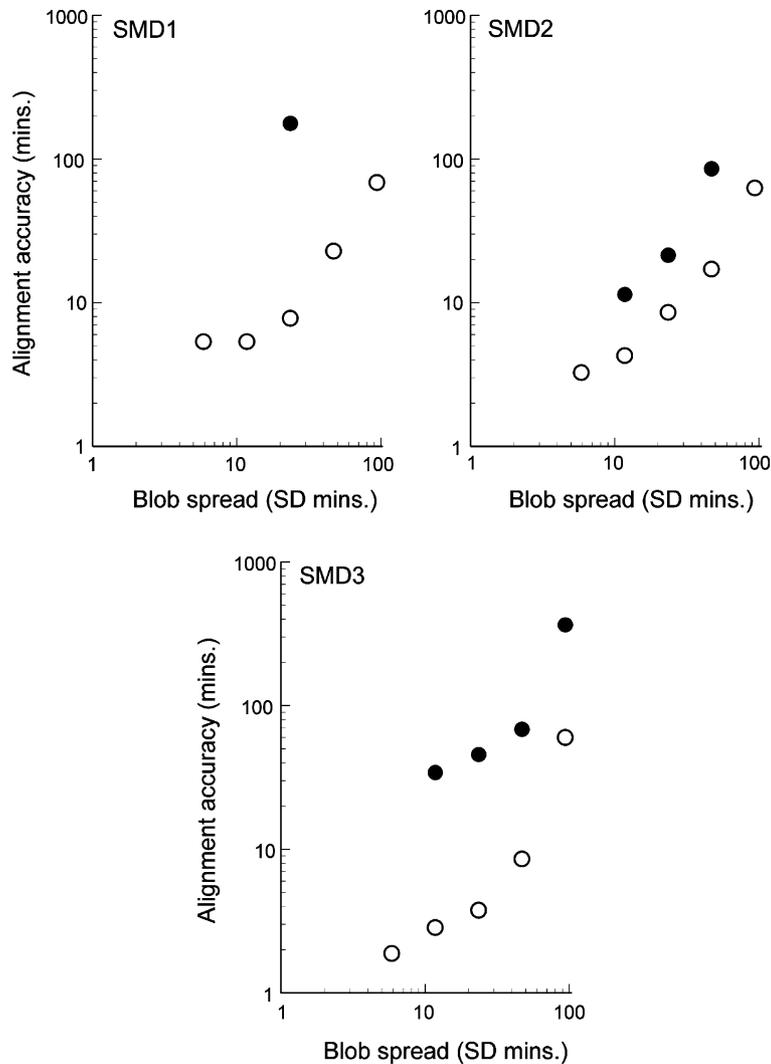


Fig. 4. Alignment accuracy in min of arc of the two eyes of the three short-term monocularly deprived cats (SMD1, SMD2, SMD3) as a function of the spatial scale of the Gaussian blobs (blob size) expressed in terms of their standard deviation (SD in min of arc). The stimuli all had the same high contrast of 0.685. Open and closed symbols depict the performance of respectively, the non-deprived and deprived eye. Measurements were possible with the deprived eye for only one blob size for SMD1, three blob sizes for SMD2 and four for SMD3.

provides a full explanation for the alignment deficits in the deprived eye would require that the contrast of the stimuli for the two eyes be effectively equated. One way to achieve this goal would be to first establish the level of physical contrast of the stimuli as viewed by the non-deprived eye that matches their apparent contrast as seen by the deprived eye. Another approach and the one employed here, was to plot the contrast of the stimuli for the two eyes with respect to their respective contrast thresholds, thereby permitting examination of the effects of stimulus contrasts for the two eyes that were incremented by the same amount (e.g. 10dB) from their respective contrast thresholds.

To permit this comparison it was necessary to first measure the contrast thresholds for the Gaussian stimulus sets for each eye. These measurements were made for each eye of 5 animals on the jumping stand by measure-

ment of the contrast detection thresholds for those blob stimulus sets for which alignment accuracy data could be made for both eyes. A simple detection task was employed whereby animals were first trained to jump toward an aligned set of blobs as opposed to an adjacent blank field of the same mean luminance. The contrast of the set of blobs was reduced in small steps until a contrast was reached where the animal's performance fell to chance. The contrast thresholds were defined as the lowest contrast for which performance was 70% correct or better. On the basis of these measurements it was possible to plot the alignment accuracy as a function of the contrast of the stimuli for the 5 tested animals with respect to their individual contrast thresholds. The data for the two animals (N2 and the binocular data for LMD3) for which the widest range of contrasts were examined are displayed in Fig. 8. For humans,

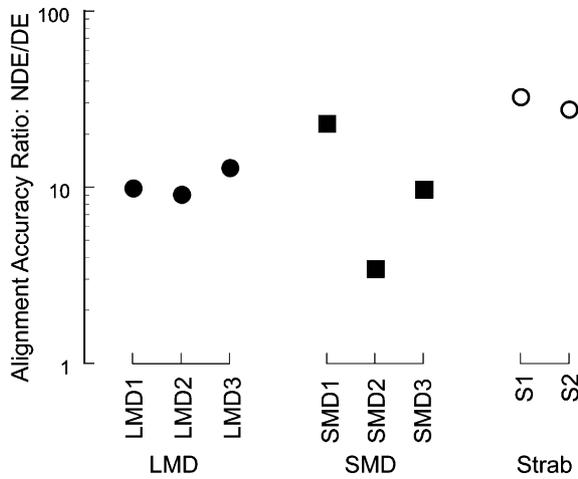


Fig. 5. The ratio of the alignment accuracy of the two eyes of each experimental animal. Legend: NDE: non-deprived eye; DE: deprived eye. Different symbols are used to depict the results from the three deprivation conditions.

the relationship between alignment accuracy and contrast when plotted on logarithmic axes can be described adequately by a line with a slope equal to the fourth-root of contrast (Hess & Holliday, 1992a). Whereas a similar linear relationship between alignment accuracy and contrast was found for both cats on logarithmic scales, the slope was greater than that observed in humans indicating a greater dependence on contrast. Indeed, power functions fitted to the data for N2 and LMD3 have slopes of 0.64 ($r = 0.98$) and 0.83 ($r = 0.95$), respectively as illustrated by the solid line through the data for N2.

In addition to the binocular data for LMD3, Fig. 8 also displays the alignment data for the deprived eye

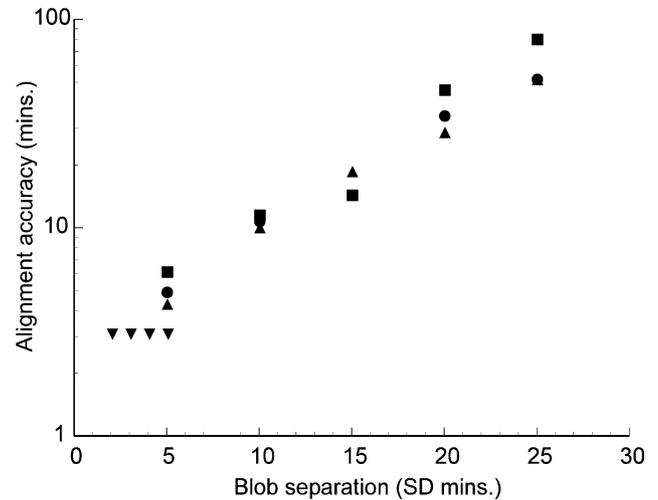


Fig. 7. Alignment accuracy in min of arc as a function of the separation of the Gaussian blobs (SD 11.46 min) expressed in terms of their standard deviation (SD). Data are shown for four animals tested with various blob separations. Legend: SMD1 (squares); S1 (circles); S2 (upright triangles); LMD3 (inverted triangles).

as a function of the contrast of the stimuli plotted with respect to its own contrast threshold. Although the alignment accuracy for stimuli having contrasts elevated similar amounts from the respective contrast thresholds for the two eyes were brought close by this manipulation at low contrasts, the values for the deprived eye were always worse and the discrepancy appeared to become larger with increasing contrast. Equivalent data for three other animals (LMD1, LMD2 and S1) with a more limited set of stimulus contrasts are displayed in Fig. 9. For LMD1 and LMD2, alignment accuracy for Gaussian blobs within 24dB of the contrast thresholds for each eye were similar but still worse for the deprived eye.

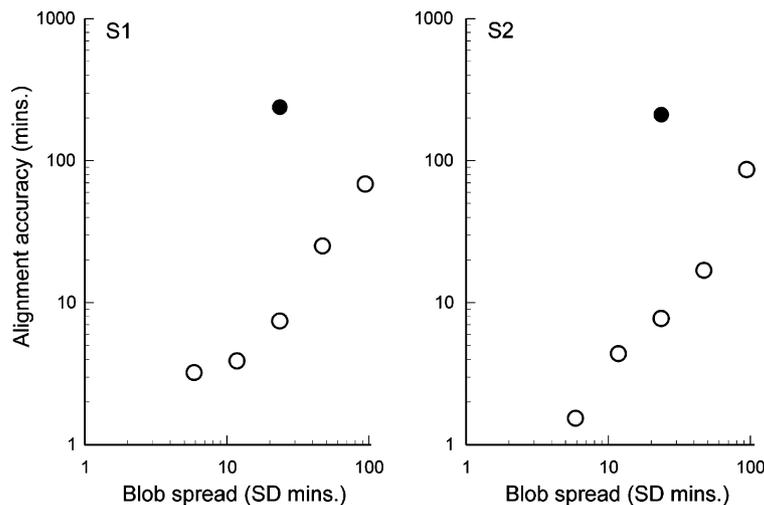


Fig. 6. Alignment accuracy in min of arc of the two eyes of the two strabismic cats (S1 and S2) as a function of the spatial scale of the Gaussian blobs (blob size) expressed in terms of their standard deviation (SD in min of arc). The stimuli all had the same high contrast of 0.685. Open and closed symbols depict the performance of respectively, the non-deviated and deviated eye. Measurements were possible with the deviated eye for only one blob size.

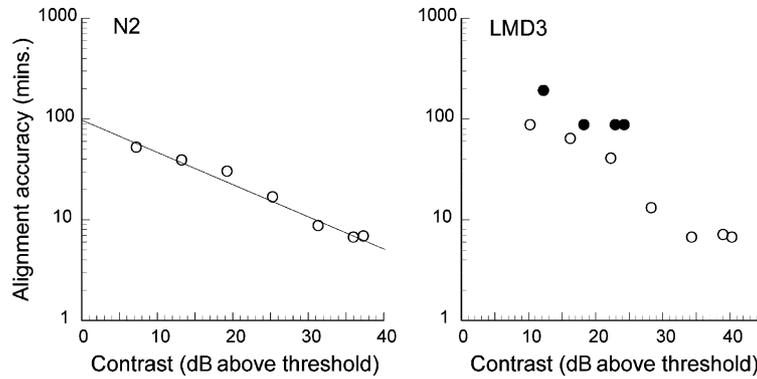


Fig. 8. Alignment accuracy in min of arc as a function of the contrast of the Gaussian blob stimuli (SD 22.9min) plotted with respect to the contrast threshold for the stimuli for each eye. Data are shown for a normal animal (N2) and the two eyes of LMD3. Open and closed symbols depict the performance of respectively, the non-deprived and deprived eye. The solid line through the data for N2 has a slope of -0.64 .

For stimuli of higher contrasts with respect to the contrast threshold of each eye, the performance of the deprived eye were worse by factors of 5–10. For the strabismic cat S1, the alignment accuracy of the deviating eye was considerably worse (by a factor of 30) than that of the other eye at all contrast levels equated with respect to their individual contrast thresholds. Thus, while at the lowest contrast levels the alignment accuracy of the deprived eye of the long-term monocularly

deprived animals approached that of the non-deprived eye at equivalent contrast levels with respect to the contrast threshold of this eye, for stimuli of higher contrasts the performance of the deprived eye was substantially worse. It therefore appears that in general, the elevated alignment accuracy thresholds of the deprived eye of monocularly deprived animals cannot be explained solely by the contrast threshold deficits of this eye. For the strabismic animal S1 it was even more apparent that

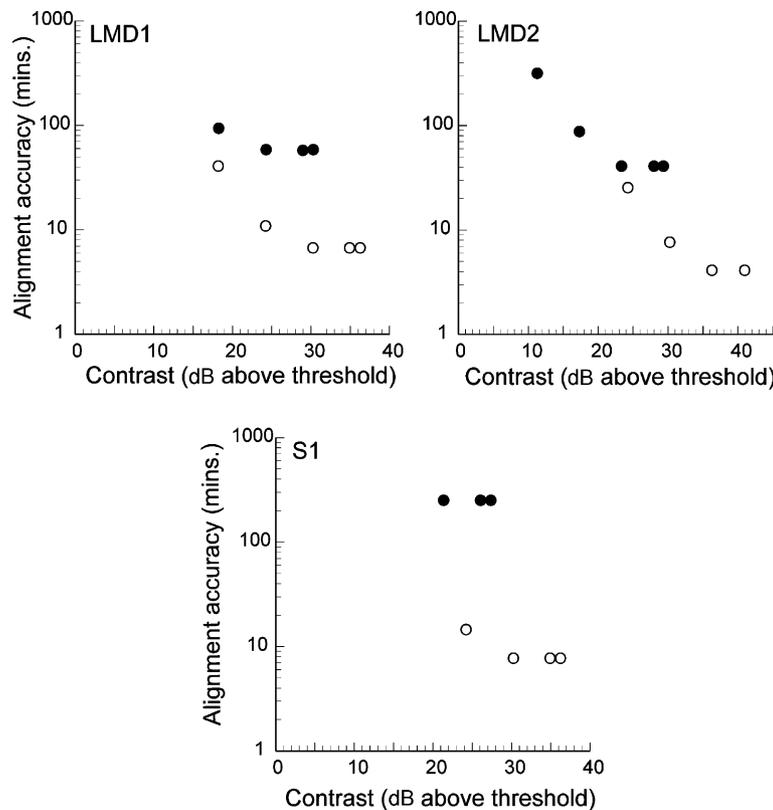


Fig. 9. Alignment accuracy in min of arc as a function of the contrast of the Gaussian blob stimuli (SD 22.9min) plotted with respect to the contrast threshold for the stimuli for each eye. Data are shown for three cats (LMD1, LMD2 and S1). Open and closed symbols depict the performance of respectively, the non-deprived and deprived (or deviated) eye.

the contrast threshold deficits were not the cause of the large elevation of alignment accuracy thresholds, a result consistent with observations made on strabismic amblyopic humans (Hess & Holliday, 1992b).

4. Discussion

4.1. Grating acuity

Despite the modification to the surgical procedure for eyelid closure that allowed for two occlusion layers as opposed to one, and the change from a detection to a discrimination task, the grating acuities of the deprived eye of the monocularly deprived and strabismic animals of this study were similar to those reported in previous studies from this laboratory (Cleland, Crewther, Crewther, & Mitchell, 1982; Giffin & Mitchell, 1978; Mitchell, 1988; Mitchell et al., 1984).

As summarized in Table 1, the deficits in the grating acuity of the deprived or deviating eye were quite small to the extent that they equaled or exceeded one octave, or a factor of two, in only two animals (S1 and LMD3). Here it is possible to emphasize a close similarity between the nature of the deficits in visually deprived animals of this study and those experienced by human amblyopes. One of the characteristic features of the latter is the variation in the severity of the deficit with the task employed for its measurement. Thus, for example, the deficits in Snellen acuity and vernier acuity can be substantially worse than those for grating acuity. Indeed it is not uncommon for contrast sensitivity functions including grating acuity to be normal in the amblyopic eye despite the fact that the subjects report substantial perceptual distortions with this eye and exhibit poor Snellen and other acuities (Barrett, Pacey, Bradley, Thibos, & Morrill, 2003; Hess et al., 1978; Howell, Mitchell, & Keith, 1983). SMD3 represents a similar example among the experimental animals as it showed poor alignment accuracy in the presence of minimal deficits

of grating acuity. As emphasized below, the deficits in alignment accuracy in all the deprived cats examined here were substantially greater than their grating acuity losses, a result that is also consistent with data from human amblyopes.

4.2. Alignment accuracy

A universal feature of the results from both normal animals and the experimental animals when tested binocularly was that alignment accuracy scaled with blob size. This result was comforting as it mirrored the performance of both normal humans and the non-amblyopic eye of human amblyopes. Even more reassuring was the large magnitude of the deficits in the alignment accuracy of the deprived or deviating eye of the experimental animals and the fact that the size of these deficits did not vary with stimulus scale. In other words, the positional abnormality was not a fixed spatial dimension for any of our animals but instead appears to be proportionally the same at all spatial scales as evidenced by the parallel displacement of the alignment accuracy thresholds for the deprived eye from the data for the other eye (Figs. 3–5). Thus, like human amblyopes, the neural representation of space of deprived cats appears to be disrupted equally at all scales.

As illustrated by the graph displayed in Fig. 5, the deficits in alignment accuracy were substantial. In terms of the ratio between the alignment thresholds for the two eyes, the deficits exceeded a factor of 9 for all but one animal (SMD2) and a factor of 20–30 for 3 animals including both of the strabismic cats. For all animals, even including SMD2 for which the deprived eye's alignment accuracy was best, the deficits exceeded by a considerable margin their grating acuity losses. This point is made evident by the graph of Fig. 10(A) in which the magnitude of the deficits in grating acuity and alignment accuracy are compared for each animal and in Fig. 10(B) where the magnitude of the deficits in contrast sensitivity and alignment accuracy are compared for

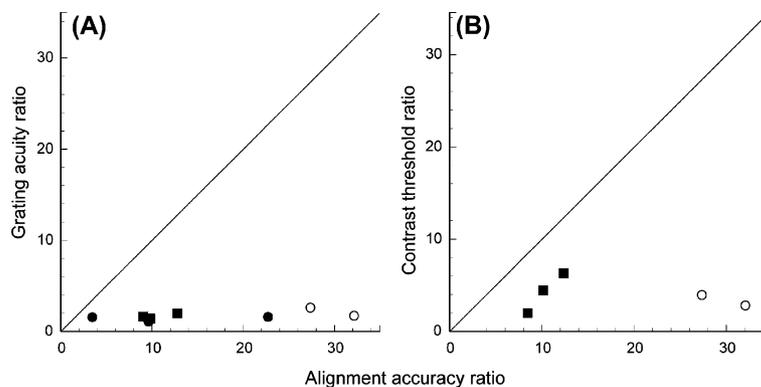


Fig. 10. The ratio of the alignment accuracy between the normal and fellow deprived or deviating eye (averaged across the scales for which measurements could be made) is plotted against either the ratio of the grating acuities of the two eyes (A) or the ratio of the contrast thresholds (B). Legend: strabismic cats (open circles); LMD cats (filled squares); SMD cats (filled circles).

the 5 animals (LMD1, LMD2, LMD3, S1 and S2) for which measurements were made of the contrast thresholds for the alignment stimuli for the two eyes in order to allow specification of the suprathreshold contrast of the stimuli for the data displayed earlier in Figs. 8 and 9. In each case, the data fall well below the line with a slope of one that represents equal deficits on both measures. Furthermore, for each of these measures (deficits for grating acuity and contrast sensitivity) there is no significant correlation (grating acuity $r = 0.49$; contrast sensitivity, $r = 0.2$) with the deficit for alignment accuracy. The fact that the deficits in alignment accuracy were so much worse and uncorrelated with either the grating acuity or contrast sensitivity losses is similar to the findings from human anisometric and strabismic amblyopes (Hess & Holliday, 1992b) and adds to the evidence that the visual losses experienced by monocularly deprived and strabismic cats represent a true model of the amblyopic defect in humans.

4.3. Comparison of the visual losses in monocularly deprived and strabismic animals

It is generally agreed that amblyopia is a heterogeneous condition with a number of identifiable types that are categorized with respect to an associated optical or oculomotor abnormality that is thought to have played a causal role. The two most common forms are anisometric and strabismic amblyopia that are associated with respectively, unequal refractive states in the two eyes or strabismus. However, a less common type has been referred to as deprivation amblyopia (von Noorden, 1967) and is typically associated with a medial opacity or other peripheral obstruction that interferes with the formation of a patterned retinal image in one or both eyes. The most common form of deprivation amblyopia in humans is associated with monocular cataract (Maurer & Lewis, 1993). With respect to the types of human amblyopia, monocular deprivation could be thought to mimic most closely the early visual experience of deprivation amblyopes.

Although there have as yet been no studies of alignment accuracy, using well-separated stimuli of the type used here, for deprivation amblyopia, studies of anisometric and strabismic amblyopes reveal fundamental differences in the underlying causes of the spatial localization deficits. Whereas for the vast majority of anisometric amblyopes the losses in alignment accuracy appear to be completely attributable to the losses of contrast sensitivity, the deficits in alignment accuracy of strabismic amblyopes appear to be uncorrelated with their contrast sensitivity losses (when stimuli with well-separated features are used) so that for them they represent independent deficits (Hess & Holliday, 1992b). In view of the precedent from studies of human amblyopes, it was important to establish the extent to which the def-

icits in alignment accuracy of monocularly deprived and strabismic cats could be attributed to their contrast sensitivity losses. There is no physical reason why poor visibility should lead to reduced positional sensitivity because the targets we use, unlike those of previous vernier studies, are virtually unaffected by the loss of high spatial frequencies that characterizes amblyopia (compare Fig. 1(C) and (D)). Any relationship that might exist must involve the mechanisms that underlie these two tasks. An investigation of this issue was conducted on the 3 long-term monocularly deprived animals (LMD1, LMD2, LMD3) and one strabismic cat (S1). When the alignment accuracy was plotted as a function of the stimulus contrast with respect to the individual contrast thresholds for the two eyes (Figs. 8 and 9), it was apparent that for the monocularly deprived animals the alignment accuracy of the deprived eye for stimuli of low to medium contrast (within 24 dB of threshold) may have been constrained by the reduced contrast sensitivity of this eye. However, for stimuli of higher contrast the performance of the deprived eye became progressively worse than that predicted on the basis of the effective contrast with respect to threshold. For the strabismic animal S1 (Fig. 9) the performance of the deviating eye was 30 times worse than that of the other eye for stimulus contrasts of equivalent magnitudes with respect to the contrast thresholds of the two eyes. Thus, for strabismic cats the deficits of alignment accuracy were not a result of the losses of contrast sensitivity. In this respect the animals reared with strabismus behaved just like human strabismic amblyopes. It was also apparent that the contrast sensitivity losses of long-term monocularly deprived cats did not provide a complete explanation for their deficits of alignment accuracy since for stimuli of high contrast the latter deficits were always substantially greater than those expected on the basis of the stimulus contrast with respect to contrast threshold. On the other hand, for stimuli of low contrast and possibly for animals monocularly deprived for short periods of time, the deficits in alignment accuracy may to a large part be attributable to the contrast sensitivity loss. However, in general, the findings from monocularly deprived cats differed from those observed in human anisometric amblyopes where in the vast majority of cases the contrast sensitivity losses predict the deficits of alignment accuracy in their entirety.

Although measurements of the alignment accuracy of kittens reared with anisometropia are necessary to strengthen the argument, the differences between the deficits of our monocularly deprived cats and those of human anisometric amblyopes reinforce the distinction that has been made between anisometric and deprivation amblyopia. On the surface, anisometropia and monocular deprivation might be considered to lie on the same continuum since eyelid closure allows some pattern information to reach the retina. Indeed, it has

been reported that it is possible to plot cortical receptive fields through the closed eyelids of one month old kittens (Spear, Tong, & Langsetmo, 1978) so that the deprivation in both monocular deprivation and anisometropia could be thought of in similar terms, namely a filtering out of high spatial frequencies from the retinal image. However, the fact that the spatial localization deficits in more severe monocularly deprived animals may be fundamentally different from those associated with anisometropia, argues against this interpretation and suggests that the two forms of deprivation may have different effects on the central visual pathways. A similar conclusion was reached earlier by Hess, France, and Tulanay-Keesey (1981) for human deprivation amblyopia.

4.4. Mixed amblyopia: the case of SMD1

Although SMD1 was deprived for only 6 days at 5 weeks of age, the deficits in alignment accuracy were substantially larger than those of the long-term monocularly deprived animals including the one deprived the longest (LMD3) to 82 days of age. The deficits for SMD1 were in fact comparable to those measured in the two animals on which esotropia was induced surgically. This finding was of particular interest as SMD1 developed esotropia in the months following termination of the period of monocular deprivation (Fig. 11). Strabismus has been reported to occur spontaneously following monocular deprivation in both kittens (Movshon, 1976; Sherman, 1972) and infant monkeys (Quick, Tigges, Gammon, & Boothe, 1989). The fact that this animal's visual performance bears some resemblance to that of the two animals on which strabismus was induced intentionally by surgery is important from several

perspectives. First, it suggests that the results from surgically induced strabismus can be generalized to strabismus that arises from other causes. And second, the results suggest that strabismus may exert a powerful effect on its own or else add to the earlier effects of monocular deprivation on the development of the visual pathways even though the deviation developed after the second month. The fact that the deficits manifested by SMD1 reflect the characteristics of strabismus suggests that this animal may represent a case of mixed amblyopia such as occurs in humans with both anisometropia and strabismus.

4.5. Relationship with vernier acuity studies

Traditionally vernier acuity targets have been used to measure positional accuracy in humans and animals with amblyopia. For the reasons that we have already outlined earlier, we do not consider such a target to be ideal. Because such a measure is likely to involve within-filter operations (Whitaker & MacVeigh, 1991), performance on such a task is affected by cues other than solely the encoding of position (Watt, 1984), one of these being contrast sensitivity (Carney & Klein, 1999). One would therefore expect a strong correlation to ensue between the deficits of positional accuracy and contrast sensitivity from its use. Unsurprisingly, this has been shown for normal animals (Kiorpes et al., 1993), humans with amblyopia (Bradley & Freeman, 1985; McKee et al., 2003) and animals with amblyopia secondary to surgically-induced strabismus or anisometropia (Kiorpes et al., 1993). A number of studies, using vernier stimuli, have shown that there is a proportional relationship between the contrast sensitivity (or grating acuity) loss (a proportional constant of unity for anisometropia and less than unity for strabismic amblyopia) and the positional loss (Barbeito, Bedell, & Flom, 1988; Levi & Klein, 1992 also see Kiorpes et al., 1993). The stimulus that we use here has been shown not to depend on such local cues (Hess & Holliday, 1992a) because of its well-separated features (Whitaker & MacVeigh, 1991). Unlike vernier acuity (Bradley & Freeman, 1985), performance on such a task in normal vision depends primarily on the size of the Gaussian envelope (not the spatial frequency spectrum), a second-order stimulus attribute (Hess & Holliday, 1992a). Thus the stimulus that we use here for the first time on normal and deprived animals represents a different approach to the assessment of positional coding than that previously provided by more traditional vernier targets and it arrives at a fundamentally different conclusion about the nature of the positional loss. Namely, that the positional loss in strabismic and deprivation amblyopia is independent of the known contrast sensitivity or acuity loss, a finding that has already been established in human amblyopes using a similar approach (Hess &

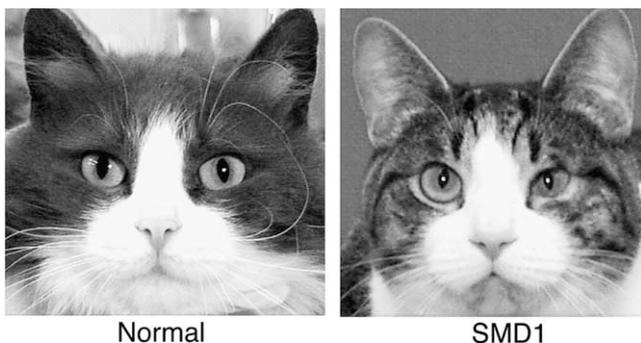


Fig. 11. A photograph of SMD1 as an adult and a normal adult cat to illustrate the esotropia that developed in the former after a 6 day period of monocular deprivation imposed at 5 weeks of age. Note that in a normal cat the pupillary axes appear divergent with respect to the optic axes as indicated by the two corneal reflexes from a distant light source. In contrast, the pupillary axes of SMD1 are convergent in relation to their position in a normal cat to the extent that they overlap with the optic axes. The photographs were taken with lights positioned in the plane of the cameras as advocated by Olson and Freeman (1978).

Field, 1994; Hess & Holliday, 1992b). Thus in both human amblyopes and in animals made artificially amblyopic there exists separate deficits for contrast sensitivity and positional sensitivity. In terms of the magnitude of the deficit, anomalous visual development of the type studied here (deprivation and strabismus) results in substantial losses to the encoding of relative position and modest deficits to visibility.

4.6. The development of normal positional accuracy

It would seem unlikely that the accuracy with which we estimate spatial distances is set solely by the fidelity of the anatomical connections that underpin the topographical projection from retina to cortex. While such topography may represent the foundations of our positional code, it is likely that positional accuracy is enhanced beyond this strict anatomical limit during development by an activity-dependent mechanism. Such a Hebbian mechanism, driven by the degree of correlation in the firing pattern of neurons, could provide additional, self-calibration to optimize positional accuracy (Hess & Field, 1994). The present losses of positional accuracy in cats whose vision is disrupted in early life due to either lid suture or strabismus could involve a disruption to this posited self-calibrating mechanism and may be better thought of as an uncalibrated neuronal disarray. This in turn leaves open the possibility that, in the normal animal, events during development may play an important role in the encoding of spatial position. To date, the only studies that have addressed this issue have used vernier targets (Shimojo et al., 1984; Shimojo & Held, 1987) that may be non-ideal because of their strong dependence on contrast sensitivity (Carney & Klein, 1999). This issue should ideally be addressed using stimuli similar to those of the present investigation where the associated effects of reduced contrast sensitivity can be adequately evaluated.

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References

Barbeito, R., Bedell, H. E., & Flom, M. C. (1988). Does impaired contrast sensitivity explain the spatial uncertainty of amblyopes? *Investigative Ophthalmology & Visual Science*, 29, 323–326.

- Barrett, B. T., Pacey, I. E., Bradley, A., Thibos, L. N., & Morrill, P. (2003). Nonveridical visual perception in human amblyopia. *Investigative Ophthalmology & Visual Science*, 44, 1555–1567.
- Bedell, H. D., & Flom, M. C. (1981). Monocular spatial distortion in strabismic amblyopia. *Investigative Ophthalmology & Visual Science*, 20, 263–268.
- Bradley, A., & Freeman, R. D. (1985). Is reduced acuity in amblyopia due to position, contrast or fixation deficits? *Vision Research*, 25, 55–66.
- Carney, T., & Klein, S. A. (1999). Optimal spatial localization is limited by contrast sensitivity. *Vision Research*, 39, 503–511.
- Cleland, B. G., Crewther, D. P., Crewther, S. G., & Mitchell, D. E. (1982). Normality of spatial resolution of retinal ganglion cells in cats with strabismic amblyopia. *Journal of Physiology*, 326, 235–249.
- Daw, N. W. (1995). *Visual development*. New York: Plenum Press.
- Demianin, R., & Hess, R. F. (1996). Positional loss in strabismic amblyopia—interrelationship of alignment threshold, bias, spatial scale and eccentricity. *Vision Research*, 36, 2771–2794.
- Freeman, R. D. (1980). Corneal radius of curvature of the kitten and the cat. *Investigative Ophthalmology & Visual Science*, 19, 306–308.
- Fronius, M., & Sireteanu, R. (1989). Monocular geometry is selectively distorted in the central visual field of strabismic amblyopes. *Investigative Ophthalmology & Visual Science*, 30, 2034–2044.
- Giffin, F., & Mitchell, D. E. (1978). The rate of recovery of vision after early monocular deprivation in kittens. *Journal of Physiology*, 274, 511–537.
- Hall, S., E & Mitchell, D. E. (1991). Grating acuity of cats measured with detection and discrimination tasks. *Behavioural Brain Research*, 44, 1–9.
- Harwerth, R. S., Smith, E. L., Boltz, R. L., Crawford, M. L. J., & von Noorden, G. K. (1983). Behavioral studies on the effect of abnormal early visual experience in monkeys: spatial modulation sensitivity. *Vision Research*, 23, 1501–1510.
- Hess, R. F. (2002). Sensory processing in human amblyopia: snakes and ladders. In M. Moseley & A. Fielder (Eds.), *Amblyopia: a multidisciplinary approach* (pp. 19–42). Oxford: Butterworth Heinemann Press.
- Hess, R. F., Campbell, F. W., & Greenhalgh, T. (1978). On the nature of the neural abnormalities in human amblyopia: neural aberrations and neural sensitivity loss. *Pflügers Archiv: European Journal of Physiology*, 377, 201–207.
- Hess, R. F., France, T., & Tulanay-Keeseey, U. (1981). Residual vision in humans who have been monocularly deprived of pattern stimulation in early life. *Experimental Brain Research*, 44, 295–311.
- Hess, R. F., & Field, D. J. (1994). Is the spatial deficit in strabismic amblyopia due to loss of cells or an uncalibrated disarray of cells? *Vision Research*, 24, 3397–3406.
- Hess, R. F., & Hayes, A. (1994). The coding of spatial position by the human visual system: effects of spatial scale and retinal eccentricity. *Vision Research*, 34, 625–643.
- Hess, R. F., & Holliday, I. A. (1992a). The coding of spatial position by the human visual system: effects of spatial scale and contrast. *Vision Research*, 32, 1085–1097.
- Hess, R. F., & Holliday, I. A. (1992b). The spatial localization deficit in amblyopia. *Vision Research*, 32, 1319–1339.
- Howell, E. R., Mitchell, D. E., & Keith, C. G. (1983). Contrast thresholds for sine gratings of children with amblyopia. *Investigative Ophthalmology & Visual Science*, 24, 782–787.
- Kiorpes, L. (1992). Effect of strabismus on the development of vernier acuity and grating acuity in monkeys. *Visual Neuroscience*, 9, 253–259.
- Kiorpes, L., Kipers, D. C., & Movshon, J. A. (1993). Contrast sensitivity and vernier acuity in amblyopic monkeys. *Vision Research*, 33, 2301–2311.
- Kiorpes, L., & McKee, S. P. (1999). Neural mechanisms underlying amblyopia. *Current Opinion in Neurobiology*, 9, 480–486.

- Kiorpes, L., Tang, C., Harken, M. J., & Movshon, J. A. (2003). Ideal observer analysis of the development of spatial contrast sensitivity in macaque monkeys. *Journal of Vision*, 3, 630–641.
- Lagrèze, W. D., & Sireteanu, R. (1991). Two-dimensional spatial distortions in human strabismic amblyopia. *Vision Research*, 31, 1271–1288.
- Lehmkühle, S., Kratz, K. E., & Sherman, S. M. (1982). Spatial and temporal contrast sensitivity of normal and amblyopic cats. *Journal of Neurophysiology*, 48, 372–387.
- Lennie, P., Trevarthen, C., VanEssen, D., & Wassle, H. (1989). Parallel processing of visual information. In L. Spillmann & J. S. Werner (Eds.), *Visual perception. The Neurophysiological Foundations* (pp. 103–128). San Diego: Academic Press.
- Levi, D. M., & Carkeet, A. (1993). Amblyopia: a consequence of abnormal visual development. In K. Simons (Ed.), *Early visual development, normal and abnormal* (pp. 391–408). New York: Oxford University Press.
- Levi, D. M., & Klein, S. A. (1985). Vernier acuity, crowding and amblyopia. *Vision Research*, 25, 979–991.
- Levi, D., & Klein, S. A. (1992). The role of local contrast in the visual deficits of humans with naturally occurring amblyopia. *Neuroscience Letters*, 135, 63–66.
- Levi, D. M., Klein, S. A., & Yap, Y. (1987). Positional uncertainty in peripheral and amblyopic vision. *Vision Research*, 27, 581–597.
- Maurer, D., & Lewis, T. L. (1993). Visual outcomes after infantile cataract. In K. Simons (Ed.), *Early visual development, normal and abnormal* (pp. 454–484). New York: Oxford University Press.
- McKee, S. P., Levi, D. M., & Movshon, J. A. (2003). The pattern of visual deficits in amblyopia. *Journal of Vision*, 3, 380–405.
- Mitchell, D. E. (1988). The extent of visual recovery from early monocular or binocular visual deprivation in kittens. *Journal of Physiology*, 395, 639–660.
- Mitchell, D. E. (1991). The long-term effectiveness of different regimens of occlusion on recovery from early monocular deprivation in kittens. *Philosophical Transactions of the Royal Society of London, Series B*, 333, 51–79.
- Mitchell, D. E., Cynader, M., & Movshon, J. A. (1977a). Recovery from the effects of monocular deprivation in kittens. *Journal of Comparative Neurology*, 176, 53–64.
- Mitchell, D. E., Giffin, F., & Timney, B. (1977b). A behavioral technique for the rapid assessment of the visual capabilities of kittens. *Perception*, 6, 181–193.
- Mitchell, D. E., Giffin, F., Wilkinson, F., Anderson, P., & Smith, M. L. (1976). Visual resolution in young kittens. *Vision Research*, 16, 363–366.
- Mitchell, D. E., Ruck, M., Kaye, M. G., & Kirby, S. (1984). Immediate and long-term effects on visual acuity of surgically induced strabismus in kittens. *Experimental Brain Research*, 55, 420–430.
- Movshon, J. A. (1976). Reversal of the behavioural effects of monocular deprivation in the kitten. *Journal of Physiology*, 261, 175–187.
- Murphy, K. M., & Mitchell, D. E. (1987). Reduced visual acuity in both eyes of monocularly deprived kittens following a short or long period of reverse occlusion. *Journal of Neuroscience*, 7, 1526–1536.
- Murphy, K. M., & Mitchell, D. E. (1991). Vernier acuity of normal and visually deprived cats. *Vision Research*, 31, 253–266.
- Olson, C. R., & Freeman, R. D. (1980). Profile of the sensitive period for monocular deprivation in kittens. *Experimental Brain Research*, 39, 17–21.
- Olson, C. R., & Freeman, R. D. (1978). Eye alignment in kittens. *Journal of Neurophysiology*, 141, 848–859.
- Quick, M. W., Tigges, M., Gammon, J. A., & Boothe, R. G. (1989). Early abnormal visual experience induces strabismus in infant monkeys. *Investigative Ophthalmology & Visual Science*, 30, 1012–1017.
- Sherman, S. M. (1972). Development of interocular alignment in cats. *Brain Research*, 37, 187–203.
- Shimojo, S., Birch, E. E., Gwiastza, J., & Held, R. (1984). Development of vernier acuity in infants. *Vision Research*, 24, 721–728.
- Shimojo, S., & Held, R. (1987). Vernier acuity is less than grating acuity in 2- and 3-month olds. *Vision Research*, 27, 77–86.
- Spear, P. D., Tong, L., & Langsetmo, A. (1978). Striate cortex neurons of binocularly deprived kittens respond to visual stimuli through the closed eyelids. *Brain Research*, 155, 141–146.
- Toet, A., & Koenderink, J. J. (1988). Differential spatial displacement discrimination thresholds for Gabor patches. *Vision Research*, 28, 133–143.
- Toet, A., von Eekhout, M. P., Simons, H. L. J., & Koenderink, J. J. (1987). Scale invariant features of differential spatial displacement discrimination. *Vision Research*, 27, 441–452.
- von Noorden, G. K. (1967). Classification of amblyopia. *American Journal of Ophthalmology*, 63, 238–244.
- Wandell, B. A. (1995). *Foundations of vision*. Sunderland, MA: Sinauer.
- Watt, R. J. (1984). Towards a general theory of visual acuities for shape and spatial arrangement. *Vision Research*, 24, 1377–1386.
- Weiss, C., Rentschler, I., & Caelli, T. (1985). Amblyopic processing of positional information Part II: Sensitivity to phase distortion. *Experimental Brain Research*, 60, 279–288.
- Wilson, H. R. (1991). Model of peripheral and amblyopic hyperacuity. *Vision Research*, 31, 967–982.
- Whitaker, D., & MacVeigh, D. (1991). Interaction of separation and spatial frequency in vernier acuity. *Vision Research*, 31, 1205–1212.