

Contrast Sensitivity and Vernier Acuity in Amblyopic Monkeys

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Human psychophysical studies suggest that strabismic and anisometric amblyopes may have characteristically different patterns of visual loss. In particular, anisometric amblyopes often show deficits on spatial localization tasks that scale with their spatial resolution losses, whereas strabismic amblyopes can show localization deficits that are large relative to their losses in spatial resolution. We have compared the performance of non-human primates with experimentally-induced anisometric and strabismic amblyopia on contrast detection and vernier acuity tasks. The performance of both groups of animals was fundamentally similar: both strabismic and anisometric monkeys showed deficits in spatial localization that were large relative to their resolution losses, although the animals with the most disproportionate losses were strabismic. We investigated the extent to which contrast sensitivity losses accounted for the vernier acuity deficits. The results showed that, in most cases of either strabismic or anisometric amblyopia, when the vernier stimuli for each eye were equated in terms of effective contrast, the extent of the vernier acuity deficit was reduced to approximately the extent of the spatial resolution deficit. In two cases, both of strabismic amblyopia, we found that equating the stimuli in this way was not sufficient to make the deficits equal, a pattern that has been described for human strabismic amblyopes.

Contrast sensitivity Vernier acuity Strabismus Anisometropia Amblyopia

INTRODUCTION

Amblyopia occurs in association with both strabismus and anisometropia. In recent years, a number of psychophysical studies have found differences in the characteristics of the amblyopias associated with strabismus and anisometropia in humans. Hess, Campbell and Zimmern (1980) reported that strabismic amblyopia *normalizes*, i.e. the extent of the amblyopia diminishes, under conditions of reduced illumination whereas anisometric amblyopia does not. Contrast perception, as measured by contrast matching, is normal at suprathreshold levels of contrast for strabismic amblyopes, but may remain abnormal over a range of suprathreshold contrasts in anisometric amblyopes (Hess & Bradley, 1980; Hess, Bradley & Piotrowski, 1983). Both types of amblyopes also show deficits on a wide variety of spatial localization tasks; the localization deficits of anisometric amblyopes are typically proportional to their deficits in spatial resolution while those of strabismic amblyopes are not (see, e.g. Levi & Klein, 1985).

The large localization deficits shown by some strabismic amblyopes have prompted speculation about spatial organization in the amblyopic visual system. Three

related sources of spatial confusion that have been suggested are *spatial undersampling*, *spatial scrambling*, and *positional uncertainty* (see Bennett & Banks, 1991; Levi & Klein, 1990; Wilson, 1991; Watt & Hess, 1987; Hess & Watt, 1990, for discussions). The idea of spatial undersampling in the amblyopic fovea suggests that, as in the normal peripheral retina, visual anomalies associated with aliasing might limit performance (Levi & Klein, 1985; see also Tiana, Williams, Coletta & Haake, 1991; Anderson & Hess, 1990). Spatial scrambling and positional uncertainty both refer to the possibility that there is local disorder to the sampling mosaic. Several models have suggested that human observers do not “know” the precise position of their cones outside the fovea (e.g. Hirsch & Hylton, 1984), and the concept of spatial position uncertainty in amblyopes simply extends this notion to the fovea. Spatial scrambling is a variant of this idea, originally proposed by Hess, Campbell and Greenhalgh (1978), to explain the perceptual “jumbling” or “crowding” often reported by amblyopes. The suggestion here is that in addition to not being aware of the precise location of their visual receptive fields, amblyopes systematically *mislocalize* them, therefore imposing neural topographic disorder on visual patterns.

The psychophysical evidence in support of the idea of spatial confusion operating in amblyopia is conflicting. It is generally accepted that localization deficits in strabismic amblyopia can be more severe than expected from other measures (Bedell, Flom & Barbeito, 1985;

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Barbeito, Bedell & Flom, 1988). Levi *et al.* have found that losses in localization ability for anisometric amblyopes can be accounted for by considering the reduced spatial frequency and contrast sensitivity of the amblyopic visual system, modeled by internal blur, without additional spatial confusion (Levi, Klein & Yap, 1987; Levi & Klein, 1990). On the other hand, Watt and Hess (1987) and Pointer and Watt (1987) argue that internal blur is not sufficient to model even anisometric amblyopia, and that positional uncertainty and spatial scrambling are a component of both forms of amblyopia. Hess and Holliday (1992) have recently extended this idea to argue that all strabismic and some anisometric amblyopes have localization deficits that are metrically unrelated to their contrast sensitivity deficits.

There are important limitations on the interpretation of data showing differences between groups of human amblyopes. For one thing, amblyopes are typically classified on the basis of the associated conditions they show at the time of testing, and complete clinical histories are rarely available to verify that these conditions have obtained throughout life. Because both strabismus and anisometropia can themselves *arise* as a result of visual neural disorders (von Noorden, 1980), it is conceivable that some of the associations observed between patterns of amblyopia and strabismus or anisometropia exist in part because the amblyopia may provoke or alter these conditions. There is, for example, evidence that refractive errors measured in young individuals are not maintained throughout life, and that the incidence of anisometropia in the young population may be lower than expected from the incidence of "anisometric" amblyopia in adults (Almeder, Peck & Howland, 1990). A related issue is that strabismus is itself often associated with anisometropia, so that individuals classified as strabismic may in fact have multiple abnormalities. A final problem is that the populations of amblyopes tested are often small and may be idiosyncratic. Preliminary data from an ongoing large-scale classification study of human amblyopes do not reveal the strabismic/anisometric distinction expected from earlier work (Hsu-Winges, McKee, Schor, Wilson, Steinman, Koch, Davis, Day, Movshon, Flom, Levi & Flynn, 1991; McKee, Schor, Steinman, Wilson, Koch, Davis, Hsu-Winges, Day, Chan, Movshon, Flom, Levi & Flynn, 1992).

To understand the amblyopic visual system in detail, it is important to identify the neural correlates of the psychophysical deficits; this may only be done directly in an animal model. The use of the animal model also has the virtue that the visual experience and clinical history of the subjects can be controlled and completely known. Numerous studies have demonstrated that the macaque monkey is an excellent model for human strabismic (von Noorden & Dowling, 1970; Harwerth, Smith, Boltz, Crawford & von Noorden, 1983; Kiorpes & Boothe, 1980; Kiorpes, Carlson & Alfi, 1989; Kiorpes, 1992b) and anisometric (Boothe, Kiorpes & Hendrickson, 1982; Smith, Harwerth & Crawford, 1985; Kiorpes, Boothe, Hendrickson, Movshon, Eggers &

Gizzi, 1987) amblyopia. These studies have demonstrated that monkeys reared with experimentally-produced strabismus or anisometropia develop amblyopia, as measured by acuity or contrast sensitivity, that is similar in frequency, character, and severity to that seen in the human population. In addition, Kiorpes (1992b) found that experimentally strabismic monkeys show a greater deficit in spatial position sensitivity than in spatial resolution as do strabismic humans.

In the present study, we compared the performance of monkeys with anisometric or strabismic amblyopia on vernier acuity, spatial resolution and contrast sensitivity tasks. We found the visual characteristics of the two groups of animals to be rather similar. Both strabismic and anisometric monkeys showed deficits in spatial localization, resolution, and contrast sensitivity. Anisometric as well as strabismic amblyopes typically had localization deficits that were large relative to their resolution losses. When the vernier stimuli for each eye were equated in terms of effective contrast, the extent of the vernier acuity deficit was reduced to approximately the extent of the spatial resolution deficit in most subjects, though some strabismic amblyopes showed a residual deficit. It therefore appears that the distinction between different types of amblyopia may not simply be associated with the distinction between strabismus and anisometropia—it may be that some amblyopes have a distinctive pattern of deficits, and this pattern is more likely to emerge after strabismus than after anisometropia.

METHODS

Subjects

Twelve amblyopic pigtailed macaques, *Macaca nemestrina*, participated in this study. They were hand-raised from infancy in our primate nursery, or in the nursery of the Washington Regional Primate Center where they were born. Three monkeys were raised with unilateral esotropia produced surgically; four were raised with unilateral esotropia produced by neurotoxin injection; and five were raised with unilateral defocus, one case of which was natural. Control data were obtained from eight monkeys raised normally. Care of the animals was provided in accordance with established, approved protocols, which conform to the *NIH guide for the care and use of laboratory animals*. Clinical data on the monkeys are presented in Table 1, where onset age corresponds to the age at which the experimental condition was begun. Note that the refractive errors listed are those observed during the rearing period. In one strabismic case (AM), anisometropia existed during the rearing period and persisted—in fact increased—over the long term. Some data from some of these animals have been presented elsewhere (Kiorpes *et al.*, 1989; Kiorpes, 1992b; Kiper, 1993).

Experimental strabismus

Esotropia was induced either by injection of *Clostridium botulinum A* neurotoxin or by surgical alteration of the horizontal rectus muscles. In the neurotoxin case,

TABLE 1. Clinical data on the amblyopic monkeys

Subject	Onset age (days)	Refractive error		Deviation (Δ)
		Right eye	Left eye	
AM (TS)	32	+2.00	+4.00	25
AN (TS)	31	+5.00	+6.00	20
JS (TS)	26	+5.50 + 0.50 \times 180	+5.25 - 0.25 \times 180	35
OD (TS)	22	+3.50 - 0.25 \times 180	+3.75 - 1.00 \times 120	30
GH (SS)	45	+1.00 + 0.50 \times 90	+1.00 + 0.50 \times 90	20
FT (SS)	22	+1.75	+1.75 + 0.25 \times 180	25
HC (SS)	86	+2.00	+2.25 + 0.50 \times 180	10
FP (A)	19	+6.00	+5.00	
FR (A)	18	-0.25	-0.25	
LF (A)	10	+8.75	+8.75	
OC (A)	25	+3.50 - 0.25 \times 180	+3.50	
VZ (NA)	*	+1.75	+5.50 - 0.50 \times 180	

Age at induction of esotropia (TS, toxin-induced; SS, surgically-induced) or anisometropia (A) (NA, natural anisometropia, *noted at age 5 months) and refractive status during rearing are listed for each animal. The angle of esotropia (to the nearest 5 Δ) as measured during the first 6 months after induction.

C. botulinum A was injected into the lateral rectus muscle of the left eye (Scott, Rosenbaum & Collins, 1973; see also Kiorpes *et al.*, 1989). The lateral rectus was exposed by dissection of the conjunctiva; the neurotoxin was injected under visual control with additional EMG guidance via the injection needle. The dosage delivered was usually 7–10 units (0.05 ml vol.) of *C. botulinum A* toxin per injection. Injections were made while the monkey was sedated with ketamine hydrochloride. In two cases, AN and AM, ptosis developed following the injection that at least partially obscured the pupil for 10–13 days. The other animals were given an injection of botulinum antitoxin (1.6×10^{-3} units; 0.2 ml vol.) into the superior medial region of the orbit prior to the neurotoxin injection in order to reduce the likelihood of subsequent ptosis (Scott, 1987). The pattern of data from subjects who developed a ptosis was identical to those that did not, suggesting that the short period of ptosis had little or no effect on the results. However, it may be noteworthy that these two animals had the poorest grating acuities in the strabismic group. The creation of surgical strabismus involved transection of the lateral rectus muscle and resection of the medial rectus muscle of the left eye. The medial rectus was, in addition, advanced to the limbus. Surgery was carried out under ketamine hydrochloride sedation using sterile surgical techniques.

The resulting esotropia using these methods is typically of a moderate extent, ranging from 10 to 40 Δ estimated by the Hirschberg method from photographs (Kiorpes *et al.*, 1989). The angle of deviation measured during the first 6 months after induction of esotropia is listed in Table 1 for each strabismic subject. Note that the extent of the esotropia in the neurotoxin cases tends to decrease over time while in the surgical cases it tends to remain constant or even increase (Kiorpes *et al.*, 1989).

Experimental anisometropia

Anisometropic amblyopia was created by inserting a -10 D extended-wear soft contact lens in the right eye

and a plano lens in the left. Lenses were 70% water content made by Contact Lens Precision Labs, Ltd, Cambridge, England. The monkey wore the lenses beginning 10–25 days after birth. Unilateral defocus was imposed for 7–10 months. The status and condition of the lenses was checked at 4 hr intervals from 7 a.m. to 11 p.m. daily (the room was dark at other times). If a lens was out, or any sign of abnormality was noted, the lens was replaced immediately. In addition, the lenses were routinely changed and cleaned weekly. A representative lens-wear record is shown in Fig. 1. The amount of time the -10 D (solid line) and plano (dashed line) lenses were out per week over the rearing period is shown for monkey FP. Note that since lenses were checked at 4 hr intervals, any lens out episode was automatically assigned a 4 hr duration. Thus these estimates represent the maximum possible time that the lens was out. In every case, the plano lens was out more frequently than the -10 D lens. Regular ophthalmic examinations were performed to insure the health of the eyes. No obvious strabismus was apparent during the rearing period in any of the lens-reared animals. However, one animal (LF) developed a large angle exotropia following the rearing period.

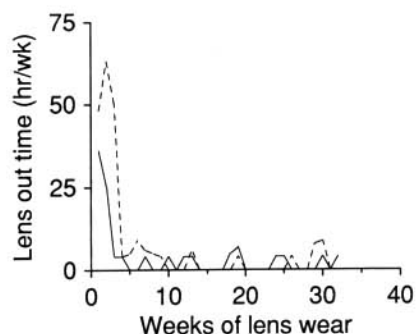


FIGURE 1. A summary of the lens-rearing records for a typical anisometropic monkey (FP), showing the proportion of time for which we were certain the monkey wore the blurring contact lens throughout the period of experimental anisometropia. The dashed line shows data for the eye with the plano lens, the solid line show data for the eye with the -10 D lens.

Behavioral testing

The animals were trained to perform an operant two-alternative forced-choice discrimination task. Training and testing procedures used have been described in detail previously (Williams, Boothe, Kiorpes & Teller, 1981; Kiorpes, 1992a). Briefly, the animals were placed in a testing cage from which they viewed the stimuli and responded by pulling one of two grab bars located within their reach. The monkeys were rewarded with 0.25 ml of apple juice for correct discriminations; errors were followed by a time out period, usually 5–10 sec in duration, that was signaled by a tone. Each animal was trained and tested on both contrast sensitivity and vernier acuity tasks. Each eye was tested independently for each animal. Optical correction was provided as needed based on behaviorally established best refraction (see Kiorpes & Boothe, 1984). The animals were all visually mature (more than 1 yr of age) at the time the measurements reported in this paper were made.

For measuring contrast sensitivity functions, sinusoidal gratings were generated on a pair of Joyce Electronics DM-2 displays (white phosphor) controlled by a PDP-11 computer. The luminance of the Joyce displays was 250 cd/m². Each screen was visible through a circular aperture that subtended 6–12 deg depending on the viewing distance, which ranged from 0.9 to 1.8 m depending on the animals' resolution range. The task required the animal to discriminate the grating from a homogeneous field matched in space-average luminance to the grating. Spatial frequency and contrast of the grating target were varied to define the resolution range of the animal. For most contrast sensitivity functions, five contrast values for each of 4–6 spatial frequencies were presented in pseudorandom order. Each contrast sensitivity estimate is based on 40 trials per stimulus condition.

For vernier acuity testing, stimuli were a pair of clearly visible vertical square-wave gratings; within one of the gratings, alternating sections of the grating were offset horizontally (Kiorpes, 1992a). The animals' task was to discriminate the grating containing the offset portions from the unaltered grating; grating contrast was either kept constant near 100% or was varied over blocks of trials. The vernier stimuli were presented on either a Barco CCID 7351 monitor or a pair of Nanao 3030 black-and-white displays controlled by a personal computer. The Nanao screens each subtended 2–8 deg at viewing distances ranging from 2 to 8 m. Their luminance was 30 cd/m². The luminance of the Barco monitor was 42 cd/m²; the screen subtended 13–25 deg for viewing distances ranging from 0.75 to 1.5 m. The vernier acuity stimuli were scaled according to the resolution range of the eye being tested. The fundamental frequency was chosen to be near the peak of the contrast sensitivity function: usually 1–2 c/deg for amblyopic eyes and 2–4 c/deg for non-amblyopic eyes. The height of the offset portions was usually equal to the spatial period of the grating, ranging from 20 to 80 min arc high.

In the study of vernier acuity as a function of contrast, the Barco display was used. The stimuli were grating patches, configured as described above, vignetted by a two-dimensional spatial Gaussian ($\sigma = 0.75$ deg), one presented on either side of the screen. Each vernier acuity estimate was based on at least 50 trials at each of five offset values. Contrast sensitivity for the fundamental frequency of the base grating for each eye was independently measured on the Barco display and used for the normalization described in the Results section.

Data analysis

All threshold estimates were obtained using method of constant stimuli. Threshold was defined as the contrast or vernier offset supporting discrimination by the subject at the 75% correct level. Threshold values and standard errors of estimate were obtained by Probit analysis of the log transformed data sets (Finney, 1971) using a maximum-likelihood-ratio technique.

To define the contrast sensitivity function, the reciprocal of threshold contrast (contrast sensitivity) and the standard error of estimate at each spatial frequency are plotted as a function of spatial frequency on log-log coordinates. A double-exponential function, defined as follows, is fit to the data:

$$k_s(\omega k_\omega)^\alpha e^{-\beta \omega k_\omega}$$

where ω is spatial frequency. The four free parameters affect primarily the steepness of the low frequency (α) and high frequency (β) portions of the curve, lateral shifts along the frequency axis (k_ω), and vertical shifts along the sensitivity axis (k_s). This function accounts well for our contrast sensitivity data in monkeys (Williams *et al.*, 1981; Boothe, Kiorpes, Williams & Teller, 1988; Kiorpes, 1989). Estimates of spatial resolution were obtained from extrapolation of the curves to a sensitivity of 1.

RESULTS

Spatial contrast sensitivity

Contrast sensitivity data from animals raised with strabismus or anisometropia are shown in Figs 2 and 3. The results were consistent across groups: the contrast sensitivity function (CSF) for the amblyopic eye was shifted both to lower levels of contrast sensitivity and lower spatial frequencies relative to the fellow non-amblyopic eye. In all cases the amblyopic eye was the eye that had received the experimental treatment, either strabismus surgery or the -10 D contact lens. Figure 2(A, B) shows CSFs from two strabismic amblyopes; Fig. 2(C, D) shows data from two anisometropic amblyopes. Open symbols represent data from the non-amblyopic eyes; solid symbols represent data from the amblyopic eyes. The similarity of the pattern of contrast sensitivity loss among these amblyopes is apparent. Contrast sensitivity data from the natural anisometropes are shown in Fig. 3; her sensitivity deficit is of the same form as that of the experimental

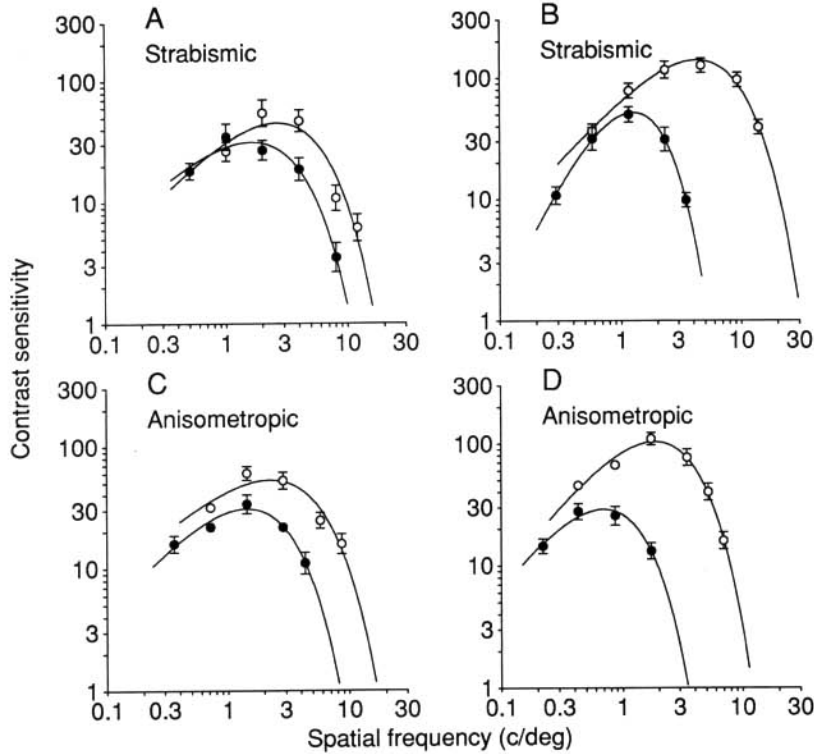


FIGURE 2. Spatial contrast sensitivity functions for four monkeys with experimentally-induced amblyopia. Solid symbols show data from the amblyopic eyes and open symbols show data from the fellow eyes. (A, B) Data for two strabismic amblyopes (monkeys JS and AN, respectively). (C, D) Data for two lens-reared anisotropic amblyopes (monkeys FR and FP, respectively). The smooth curves fit to the data are described in the Methods section.

amblyopes. In most cases, there was a modest interocular sensitivity difference at low spatial frequencies, and a progressively larger difference at higher spatial frequencies. Because of this high-frequency loss, these animals typically showed substantial interocular differences in spatial resolution (defined as the spatial frequency at which the extrapolated contrast sensitivity function falls to 1).

It is important to note that in this paper we describe data only for amblyopic animals: those having significant interocular differences in contrast sensitivity and grating acuity. We have occasionally seen animals raised using regimes similar to those reported here without producing any reliable difference in visual performance

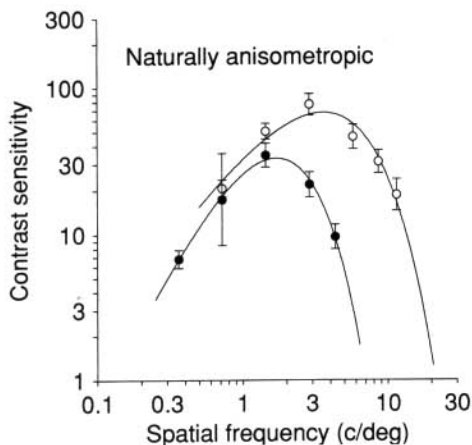


FIGURE 3. Spatial contrast sensitivity functions for the two eyes of a naturally anisotropic monkey (VZ). Format as in Fig. 2.

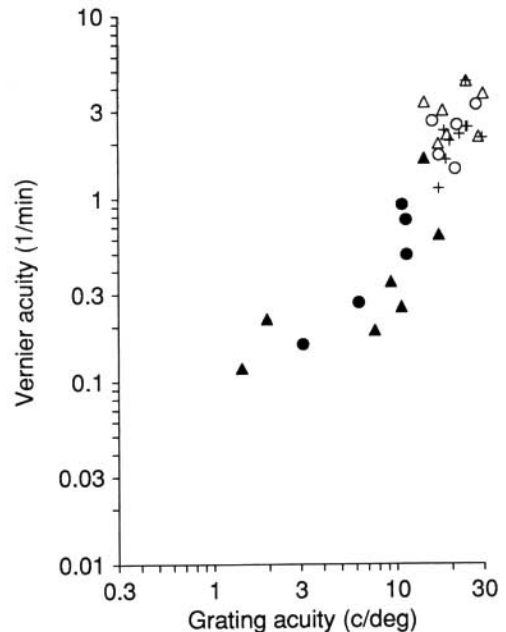


FIGURE 4. The relationship between vernier acuity and grating acuity is shown for eight normal monkeys (plus signs), the amblyopic eyes of seven strabismic (solid triangles) and five anisotropic (solid circles) monkeys, and the fellow eyes of these strabismic (open triangles) and anisotropic (open circles) monkeys. Grating acuity values were obtained by extrapolation to a sensitivity of 1 of smooth curves fit to spatial contrast sensitivity data like those shown in Figs 2 and 3. Vernier acuity values were obtained either from measurements using 100% contrast stimuli or from the 100% points of curves fit to data describing vernier acuity as a function of contrast (see below and Fig. 6).

TABLE 2. Grating and vernier acuity values for each monkey for their non-amblyopic (NA eye) and amblyopic (A eye) eyes

Subject	Grating acuity (c/deg)		Vernier acuity (l/min)		Corrected VA (l/min)
	NA eye	A eye	NA eye	A eye	NA eye
AM (TS)	14.2	2.0	3.33	0.22	
AN (TS)	17.9	1.4	3.00	0.19	1.94
JS (TS)	16.9	10.6	1.98	0.25	1.97
OD (TS)	24.1	7.6	4.35	0.19	
GH (SS)	18.9	14.1	2.21	1.64	2.08
FT (SS)	29.8	9.3	3.70	0.35	3.41
HC (SS)	28.1	17.0	2.15	0.63	1.30
FP (A)	20.9	6.2	1.44	0.27	1.15
FR (A)	17.0	11.2	1.71	0.76	1.67
LF (A)	15.7	11.1	2.63	0.49	
OC (A)	21.4	3.1	2.50	0.16	1.86
VZ (NA)	27.3	10.3	3.23	0.92	

The "corrected" vernier acuity values are corrected for the difference in contrast sensitivity between the eyes (see text for description).

between the two eyes. In this respect, monkeys resemble strabismic or anisometropic humans, some of whom do not develop amblyopia (von Noorden, 1980).

Comparison of vernier and grating acuity

In addition to spatial resolution, we measured vernier offset detection thresholds in all our monkeys. All the amblyopic subjects showed deficits in both vernier and grating acuity with their deprived eyes. The natural anisometrope, VZ, showed deficits on both measures with her more hyperopic eye. Acuity data for each amblyopic subject are given in Table 2. Figure 4 shows the relationship between vernier and grating acuity for the amblyopic and fellow eyes, as well as data from eight normally reared monkeys from another study (Kiorpes, 1992a). Solid and open symbols represent data from amblyopic and fellow eyes, respectively; plus symbols represent data from normal eyes. It is clear from these data that the two measures of acuity are not simply or proportionally related suggesting that, as in humans, measures of positional sensitivity may capture the

performance of portions of the visual system not tapped in simple contrast detection tasks.

If these two measures of acuity depend to some degree on different underlying mechanisms, it is natural to wonder whether these mechanisms are differentially affected in amblyopia. To examine this question, we compared the interocular ratios of vernier and grating acuity for each of our amblyopic subjects. Figure 5 shows the relative extent of the deficits in vernier and grating acuity for the strabismic and anisometropic monkeys in the present study. Each datum plots the ratio of the vernier acuity between the two eyes against the ratio of the grating acuity. If the deficits were equal, the data would fall near the dashed line representing equality. In fact, for both anisometropic and strabismic monkeys, the data tend to fall above the dashed line, meaning that the vernier acuity deficit was disproportionately larger than the resolution deficit in most cases. It is also evident that the data for strabismic animals (triangles) overlap those of the anisometropes (circles), although most of the animals with severe losses in vernier acuity were strabismic.

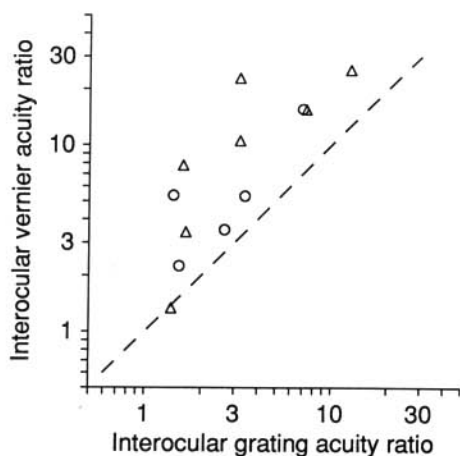


FIGURE 5. A comparison of the magnitude of the vernier and grating acuity deficits for 12 amblyopic monkeys. The ordinate plots the ratio of the vernier acuity values for the two eyes, and the abscissa plots the ratio of the grating acuity values for the two eyes. Data for normally-reared monkeys (not shown) cluster closely around a ratio of 1 on both axes (Kiorpes, 1992b).

Variation in vernier acuity with contrast

Since our monkeys showed comparable deficits in contrast sensitivity regardless of the type of amblyopia, strabismic or anisometropic, and a similar pattern of deficits in vernier and grating acuity, we wished to test the hypothesis that the deficits in vernier acuity were related directly to the contrast sensitivity deficits (Bradley & Freeman, 1985; Barbeito *et al.*, 1988; Levi & Klein, 1992). In our initial measurements, we used test stimuli whose contrast was near 100%. Because the monkeys' amblyopic eyes typically had poorer contrast sensitivity than their fellow eyes, this method might exaggerate any interocular differences by making the effective stimulus contrast lower in the amblyopic eyes. We therefore measured the relationship between vernier acuity and contrast in eight of the amblyopic monkeys, using stimuli whose contrast varied from near detection threshold to near 1.0.

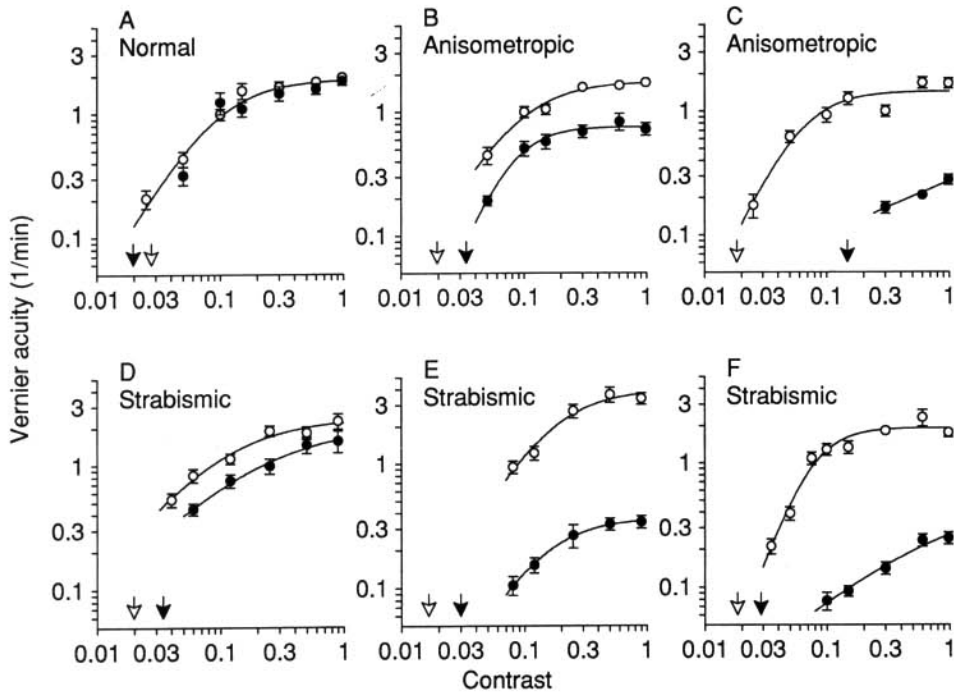


FIGURE 6. The relationship between stimulus contrast and vernier acuity for one normal monkey (A), two anisometropic monkeys (B, C: monkeys FP and FR), and three strabismic monkeys (D, E, F: monkeys GH, FT, and AN). In panels (B–F), data from the amblyopic eye are shown as solid circles, and from the fellow eye as open circles; contrast thresholds at the fundamental spatial frequency of the test targets are indicated by solid and open arrows for the amblyopic and fellow eyes, respectively. The smooth curves fit to the data are described in the text. For the normal monkey (A), the two eyes' data are shown by open and solid circles, and the single plotted curve was fitted jointly to both eyes' data.

Figure 6 shows vernier acuity as a function of contrast for six monkeys: one normal [Fig. 6(A)] two anisometropic amblyopes [Fig. 6(B, C)] and three strabismic amblyopes [Fig. 6(D, E, F)]. As before, open symbols represent data from fellow eyes and solid symbols represent data from amblyopic eyes. The arrows indicate the monkeys' contrast thresholds for sinusoidal gratings of the same fundamental spatial frequency as the vernier test targets; solid arrows show thresholds for the amblyopic eyes and open arrows show thresholds from the fellow eyes. The data are fit with a smooth curve of the form

$$k \left[\frac{C^\sigma}{C^\sigma + C_0^\sigma} \right]$$

where C is contrast, and k , σ , and C_0 are constants. As is evident from Fig. 6, this function provides a good general account of the data we obtained; it is interesting but perhaps serendipitous that it also happens to be useful in describing the contrast–response relationship of cortical neurons (Albrecht & Hamilton, 1982).

Several features of the data are noteworthy. The shapes of all the functions are similar to those reported elsewhere for humans (Watt & Morgan, 1983; Bradley & Skottun, 1987; Krauskopf & Farrell, 1991; Wehrhahn & Westheimer, 1990; Levi & Klein, 1992), although we noticed that the monkeys' data tend to saturate at high contrasts (>0.1–0.3) in a way not always seen with human data in the literature or with human observers run in our laboratory using the same stimulus conditions. The data from the normal monkey are similar to

those from the fellow eyes of the amblyopic monkeys. Many of the curves for the amblyopic eyes appear to be downward-shifted replicas of the curves for the fellow eyes [e.g. the anisometrope in Fig. 6(B) and the strabismics in Fig. 6(D, E)]; for the most severely affected animals [the anisometrope in Fig. 6(C) and the strabismic in Fig. 6(F)], the initial slope of the amblyopic eye's function appears also to be shallowed. In either pattern, the amblyopic monkeys had clear deficits in vernier acuity throughout the contrast range. Only for contrasts near detection threshold, where performance in the fellow eye falls radically, did the vernier acuity of the non-amblyopic eye sometimes approach that of the amblyopic eye.

To compensate for the different contrast sensitivities of the two eyes, we used the curves fit to the data of Fig. 6 to calculate the vernier acuity of the fellow eyes at a contrast that is the same multiple of threshold as unit contrast is for the amblyopic eye. This is equivalent to sliding the solid arrows, symbols, and associated curve in Fig. 6(B–F) so that the arrows superimpose, and using the point from the fellow eye's curve that corresponds to the endpoint of the amblyopic eye's curve. This results in a reduction in the estimated vernier acuity for the fellow eye (listed as *corrected vernier acuity* in Table 2), and a corresponding reduction in the interocular vernier acuity ratio. Because the fellow eye's performance tended to level off at high contrasts, however, the effect of this transformation was in most cases relatively subtle. Figure 7 plots the resulting interocular vernier acuity ratios relative to the interocular grating

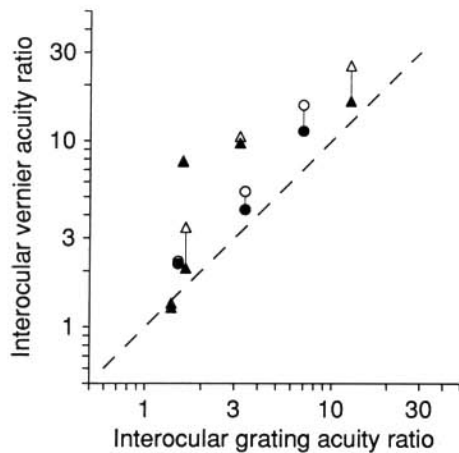


FIGURE 7. The effect of equating effective stimulus contrast on the relative magnitude of grating and vernier acuity deficits is shown for eight amblyopic monkeys, the subset of animals for which contrast-vernier measurements like those in Fig. 6 were made. Each monkey's data is represented by two data points. The upper, open symbol, taken from Fig. 5, shows the untransformed data; the lower, solid symbol is shifted to compensate for the unequal suprathreshold contrasts used in the two eyes, as described in the text. Note that the transformed filled symbols make the untransformed open symbols invisible when the effect of the transformation is small. Format otherwise as in Fig. 5.

acuity ratios for the eight amblyopic animals for which contrast vernier data were collected, using the format of Fig. 5. Each datum is now shown in two values on the ordinate: the upper, open symbol transfers the uncorrected value from Fig. 5, and the lower, solid symbol gives the "equivalent contrast" ratio. These results show that when the stimuli were equated for effective contrast, the vernier acuity deficit was in many cases reduced to approximately the same level as the deficit in spatial resolution. We conclude that the contrast sensitivity deficit does contribute to the relatively larger deficit in vernier acuity for both strabismic and anisometropic monkeys. Even after this transformation, however, there remain two individuals, both strabismic, for whom the "corrected" vernier acuity deficit was substantially larger than the grating acuity deficit. It is perhaps noteworthy that one of these animals, FT, was a surgical strabismic, while the other, JS, had her strabismus induced by the neurotoxin method.

DISCUSSION

The experiments described in this paper show that monkeys with experimental amblyopia have deficits in both spatial contrast sensitivity and in vernier acuity. As in human amblyopia, the monkeys' deficits in spatial position sensitivity are typically greater than their deficits in spatial resolution. The interpretation of this difference is not simple, however, because one would not necessarily expect the relationship between these two acuities to be strictly proportional, and Fig. 4 shows that indeed they are not. Our data show that the losses in contrast sensitivity in amblyopic eyes contribute to the relatively greater loss in vernier acuity but in cases of severe amblyopia, this is not a major factor.

One factor to consider in understanding the profile of spatial deficits in amblyopes is the relationship between vernier and grating acuity. This relationship in our amblyopic monkeys appears to be similar to that observed over the course of development in *normal* monkeys (Kiorpes, 1992a). This comparison is made in Fig. 8 where the data from Fig. 4 are mapped onto the normal developmental sequence as determined in Kiorpes (1992a). Thus the relationship between vernier and grating acuity for the amblyopic eyes of both anisometropic and strabismic monkeys is similar to that of younger normal animals. If we presume, as suggested by earlier data (Kiorpes, 1989, 1992b), that amblyopia can be understood as a slowing of visual development, then a greater deficit in vernier acuity relative to grating acuity is to be expected since vernier acuity is relatively less mature in both human and monkey infants (Shimojo & Held, 1987; Kiorpes, 1992a).

It is worth recalling that our vernier acuity task involved only the *detection* of the vernier offsets. Analysis of the spatial frequency content of our vernier display shows that the offset introduces energy at the fundamental frequency of the grating "carrier", at higher harmonics of this frequency, and at orientations other than vertical. It might be that the disproportionate loss of vernier acuity in the amblyopes therefore results from their reduced ability to detect these additional frequency components.

We explored the possibility that the reduced effective contrast of targets delivered to the amblyopic eye might account for the extra deficits in the amblyopes' position

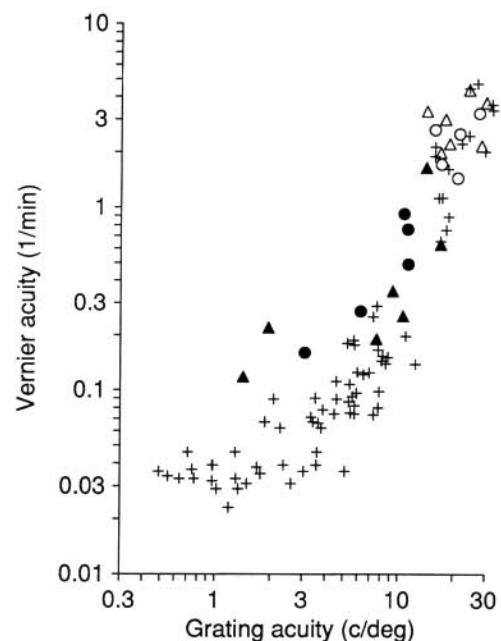


FIGURE 8. The relationship between grating and vernier acuity in the amblyopic monkeys as compared to that during normal development. Symbols and axes are the same as in Fig. 4. The normative developmental data (plus signs) are longitudinal and cross-sectional data from animals ranging in age from near birth to 1 year (Kiorpes, 1992a). Open triangles, strabismic non-amblyopic monkeys; solid triangles, strabismic amblyopic monkeys; open circles, anisometropic non-amblyopic monkeys; solid circles, anisometropic amblyopic monkeys.

sensitivity. Compensating the measurements by reducing the contrast of the targets delivered to the fellow eyes tended to make the vernier acuity losses more similar to the grating acuity losses, but in several cases substantial differences remained. It is important to appreciate that, because the curves in Fig. 6(B–F) cannot be superimposed by any horizontal shift, the interocular vernier acuity ratio is not constant across contrasts. We have chosen to make the comparison at the highest possible contrast, by analogy with the measurement of spatial resolution at maximum contrast, but other choices might lead to rather different conclusions. In particular, inspection of Fig. 6 reveals that for contrasts close to threshold, the interocular vernier acuity ratio tends to be smaller than at higher contrasts. It might be that at low contrasts near threshold, both amblyopic and fellow eyes perform poorly because many of the added frequency components are undetectable. To evaluate this idea would require application of a complete model for spatial contrast detection (e.g. Wilson, 1986), for which many of the necessary parameters are not known for our monkeys. Nonetheless, we believe that the two strabismic animals whose deficits remain disproportionate (see Fig. 7) have deficits not captured by any reasonable transformation of the contrast sensitivity measurements; this conclusion is supported by measurements showing that these and similar strabismic monkeys have deficits in spatial phase discrimination even for compound gratings whose components are clearly visible (Kiper, 1993).

In important respects, the data from our amblyopic monkeys are similar to those reported in a similar analysis of human amblyopes (Levi & Klein, 1992). Like human anisometropes, our anisometric monkeys show vernier deficits that can be accounted for by their contrast sensitivity losses. At least two of our strabismic monkeys show deficits that cannot be dealt with in this way, resembling human strabismic amblyopes. There are two main points of difference between our monkey amblyopes and human amblyopes. The first is that the vernier acuities of our monkeys' non-amblyopic eyes tend to be on the order of a factor of two or three poorer than in humans. The second is that human amblyopes typically show spatial vision profiles characteristic of the type of amblyopia, strabismic or anisometric, whereas our monkey data show less clear demarcation by etiology.

Vernier acuity for human observers typically falls in the range of 3–10 sec arc. Our monkeys' vernier performance was roughly three times worse, in the range of 10–30 sec arc. We know of no published studies of monkey vernier acuity other than our own, but because the conventional view is that macaque and human vision are quantitatively identical (e.g. DeValois, Morgan & Snodderly, 1974), this difference deserves examination. It is possible that our unconventional vernier target accounts for the difference in performance levels between monkeys and people, since most studies use a single line or edge target or a bisection task. We have, however, tested human subjects with the same target under identical viewing conditions and find vernier thresholds between 4 and 10 sec arc (Kiorpes & Movshon, 1989),

suggesting that this display is not the important factor. Moreover, we have tested several monkey subjects using conventional single-line vernier targets and have obtained acuity values similar to those reported here.

It is not unreasonable for macaque and human vision to differ quantitatively. The macaque visual system differs in both optical and neural structure from the human; in particular, the angular density of cones is lower in the fovea and changes more gradually with eccentricity (Packer *et al.*, 1990). Published measurements show contrast sensitivity and grating acuity in macaques to be lower than that of humans, in some cases by as much as a factor of two (Campbell & Green, 1965; DeValois *et al.*, 1974; Williams *et al.*, 1981; Harwerth *et al.*, 1983; see also Table 2). Moreover there are substantial variations in cone density both within and among macaque species (Perry & Cowey, 1985; Packer *et al.*, 1990; Hawken & Parker, 1991). We conclude that the quantitative differences in acuity across individuals and species are in the range of those expected; it is worth noting that the absolute value of measured acuity is less important to the analysis presented here than the pattern of spatial deficits.

The pattern of our results suggests considerable overlap between the strabismic and anisometric amblyopes. The range and pattern of contrast sensitivity deficits was similar for the two groups. Several of our *strabismic* monkeys had deficits that seemed related to contrast sensitivity losses, as did the anisometric amblyopes. One factor which may contribute to this result is the fact that the age of onset of strabismus and anisometropia in our monkeys was similar; the type and severity of amblyopia may depend on the time period during development when the abnormal conditions exist. Levi and Carkeet (1993) discuss the idea that the spatial profiles for strabismic and anisometric amblyopes are different in large part because the age of onset of anisometric amblyopia may be relatively late. As we discussed in the Introduction, it is often impossible to be certain of the precise etiology and age of onset of human amblyopias, because complete clinical histories are rarely available and classification is thus typically based on the associated conditions present at the time of testing. On the other hand, we know the clinical histories of our monkeys with some precision. In this context, it is interesting to note that preliminary results of a recent extensive study of human amblyopes reveals considerable overlap in the patterns of loss associated with strabismus and anisometropia (Hsu-Winges *et al.*, 1991; McKee *et al.*, 1992). It may be true, as is commonly believed, that both humans and monkeys show two distinct patterns of amblyopic deficit, and that these patterns are associated with different etiologies. Our data suggest, however, that the association between etiology and the pattern of deficit may be less than perfect.

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