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Influence of monocular deprivation during infancy on the later development of spatial and temporal vision

Dave Ellemberg [a], Terri L. Lewis [a,b,c,*], Daphne Maurer [a,b], Henry P. Brent [b,c]

[a] *Department of Psychology, McMaster University, 1280 Main St. West, Hamilton, Ont., Canada L8S 4K1*
[b] *The Hospital for Sick Children, Toronto, Ont., Canada*
[c] *University of Toronto, Toronto, Ont., Canada*

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Abstract

Using the method of limits, we measured spatial and temporal vision in 15 patients, aged 4–28 years, who had been monocularly deprived of patterned visual input during infancy by a dense cataract. All patients showed losses in both spatial and temporal vision, with greater losses in spatial than in temporal vision. Losses were smaller when there had been more patching of the non-deprived eye. The results indicate that visual deprivation has smaller effects on the neural mechanisms mediating temporal vision than on those mediating spatial vision. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: Visual deprivation; Unilateral congenital cataract; Development; Spatial contrast sensitivity; Grating acuity; Temporal contrast sensitivity; Critical flicker fusion frequency

1. Introduction

Children who had been visually deprived during early infancy by dense central cataracts in both eyes later show losses in both spatial and temporal vision. However, the reduction in spatial vision is much larger than the reduction in temporal vision (Ellemberg, Lewis, Maurer, Liu, & Brent, 1999). Following 1.6–8.8 months of binocular deprivation from birth, reductions in spatial contrast sensitivity occur mainly at higher frequencies, where they average 1.3 log units. Reductions in temporal vision occur only at lower frequencies, where they average only 0.4 log units. The different effects of binocular deprivation on spatial and temporal vision may be related to the slower development of spatial vision in normal children (Ellemberg, Lewis, Liu, & Maurer, 1999) and suggest that these visual functions are mediated by different neural mechanisms.

The purpose of the current study was to use the same methods to investigate the effects of monocular deprivation from a unilateral congenital cataract on the development of spatial and temporal vision. Previous studies have documented reductions in spatial vision in children with a history of such monocular deprivation, with larger reductions following monocular than binocular deprivation unless there was extensive patching of the non-deprived eye (Tytla, Maurer, Lewis, & Brent, 1988; Maurer & Lewis, 1993; Lewis, Maurer, & Brent, 1995). Those patterns of loss indicate that monocular deprivation affects the development of spatial vision both by depriving the nervous system of patterned visual input and by uneven competition for cortical connections between the deprived and non-deprived eyes, which can be reduced by extensive patching of the non-deprived eye. The pattern of loss following the combination of early deprivation and uneven competition between the eyes differs from that following early deprivation alone: unlike children treated for bilateral congenital cataract, children treated for unilateral congenital cataract show losses in spatial contrast sensitivity that decrease with increasing eccentricity and with increasing temporal modulation (Tytla et al., 1988; Tytla, Maurer, Lewis, & Brent, 1991; Maurer & Lewis, 1993; Birch, Stager, Leffler, & Weakley, 1998). The size of the deficit in spatial vision is also related to the duration of

* Corresponding author. Tel.: +1-905-5259140; fax: +1-905-5296225.
E-mail address: lewistl@mcmaster.ca (T.L. Lewis).

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monocular deprivation (Birch, Swanson, Stager, Woody, & Everett, 1993; Birch et al., 1998), although the relationship appears not to be linear and may interact with the amount of patching (Mayer, Moore, & Robb, 1989; Maurer & Lewis, 1993; Lewis et al., 1995).

Less is known about the effects of monocular deprivation on the development of temporal vision (Hess, France, & Tulunay-Keesey, 1981; Manny & Levi, 1982a,b; Tytla et al., 1988). Two studies included only patients with a history of long deprivation followed by little, if any, patching of the non-deprived eye (Hess et al., 1981; Manny & Levi, 1982a,b). In those patients, temporal contrast sensitivity to a uniform luminance field or to a sine-wave grating was reduced at all temporal frequencies with the reduction ranging from 0.2 to 1.5 log units across temporal frequencies. However, the pattern of results may differ for patients with shorter deprivation and/or better occlusion therapy. Tytla et al. (1988) measured spatial contrast sensitivity in monocularly and binocularly deprived patients with shorter deprivation using gratings that reversed in phase at a rate of 1 and 8 Hz. They found that losses in spatial contrast sensitivity decreased with increasing temporal modulation after monocular deprivation but not after binocular deprivation. However, because they tested only two temporal frequencies and because their stimuli contained both spatial and temporal information, the study did not measure responses from specific temporal channels independently of their spatial tuning.

Studies of monkeys indicate that early monocular deprivation causes larger reductions than early binocular deprivation in both spatial and temporal vision (Harwerth, Smith, Boltz, Crawford, & von Noorden, 1983a,b; Harwerth, Smith, Paul, Crawford, & von Noorden, 1991). Following 2 weeks–22 months of monocular deprivation beginning at 1 month of age, spatial contrast sensitivity was reduced by about 2.0 log units and temporal contrast sensitivity by about 0.5 log units. After comparable durations of binocular deprivation, spatial contrast sensitivity was reduced by only about 1.0 log units and temporal contrast sensitivity was normal. Unlike the results for spatial contrast sensitivity in deprived humans (Birch et al., 1993, 1998), the size of the reduction was not related to the duration of monocular deprivation, perhaps because deprivation began at 1 month of age in monkeys but not in humans, because the monocularly deprived monkeys experienced continued mild deprivation caused by uncorrected refractive errors, and/or because deprivation was not followed by any occlusion of the non-deprived eye (Harwerth et al., 1991).

The purpose of the present study was to compare spatial and temporal vision in a group of patients treated for unilateral congenital cataract at different times during the first year of life. It is well established that low level visual neurons respond to changes in luminance across both space and time (e.g. Derrington & Lennie, 1984). To separate spatial and temporal sensitivity, we measured spatial vision with static sinusoidal gratings and temporal vision with an unpatterned light source. This allowed us to measure specific spatial channels independently of their temporal tuning and to measure specific temporal channels independently of their spatial tuning.

We examined the effects of the duration of monocular deprivation ranging from 1 to 10 months on spatial versus temporal vision in patients who had patched their non-deprived eye 1.6–7 h day^{-1} throughout early childhood. This study allows the first comparison of the effects of monocular deprivation on the development of spatial versus temporal vision and, because we used the same method as our previous study of children treated for bilateral congenital cataract (Ellemberg et al., 1999b), allows an assessment of whether the effects of monocular versus binocular deprivation are the same for temporal vision as they are for spatial vision.

Using the method of limits, we studied the spatial and temporal contrast sensitivity, grating acuity, and critical flicker fusion frequency of 15 patients who had been monocularly deprived of patterned visual input during early infancy by a dense central cataract. The cataracts were treated during infancy by surgically removing the natural lens of the eye and replacing it with a contact lens to restore nearly normal visual input. We compared the results to those of 15 age-matched normal subjects tested under the same conditions.

2. Methods

2.1. Subjects

Participants were 15 patients treated for a unilateral congenital cataract and 15 age-matched controls. All age-matched controls passed a visual screening exam (for criteria, see Ellemberg et al., 1999a). Mean age at test was 12 years (range = 4.1–28.5 years). Patients were included in the study if they met all of the following criteria: (1) diagnosis of a dense central cataract in one eye on the first eye exam, which was always before 6 months of age; (2) no abnormalities in the ocular media or the retina, including no evidence of persistent hyperplastic primary vitreous; (3) no ocular disease such as glaucoma; and (4) regular contact lens wear after treatment (at least 75% of the waking time). We included patients with common associated abnormalities in the deprived eye such as strabismus, nystagmus, or microcornea and excluded patients with any abnormalities in the fellow non-deprived eye that were likely to interfere with vision (e.g. developing cataract or more than minimal refractive error). Clinical details of the patients are described in Table 1.

Table 1
Clinical details for 15 patients treated for unilateral congenital cataracts[a]

Patient (age) (sex)	Refraction[b]		Age of diagnosis/contact lenses (days)	Snellen acuity[b]	Nystagmus	Additional details
H.C. (4.1) (F)	OS[c]	+14.50	9/39	20/70	Latent OU	Strabismus surgery for LET at age 0.7 years
	OD	Piano		20/30		Patching: 5.5 h day^{-1}
B.M. (6.0) (M)	OD	+23.00	7/43	20/40	Latent OD	Strabismus surgery for LET at age 1.1 years
	OS	Plano		20/20		Patching: 3.2 h day^{-1}
M.C. (5.7) (M)	OS	+14.00	32/55	20/50	Latent OU	Strabismus surgery for LET at age 1.6 years
	OD	−1.25		20/25		Patching: 7.1 h day^{-1}
E.H. (6.6) (F)	OD	+10.75	30/56	20/30	None	No other surgery or complications
	OS	−2.50		20/25		Patching: 5.0 h day^{-1}
C.K. (6.1) (F)	OS	+13.50	15/67	20/60	Manifest OU	Strabismus surgery for LET at age 1.2 years
	OD	Plano		20/30		Patching: 4.9 h day^{-1}
D.C. (20.3) (M)	OS	+13.00	Birth/98	20/50	Latent OU	Strabismus surgery for LET at age 4.1 years
	OD	−4.50		20/15		Patching: 5.3 h day^{-1}
C.P.M. (7.4) (F)	OD	+17.00	83/116	20/200	None	Strabismus surgery for RET at age 1.0 years
	OS	Plano		20/25		Patching: 4.7 h day^{-1}
N.F. (16.4) (F)	OD	+11.50	90/124	20/50	Latent OU	Strabismus surgery for RET at age 2.3 years
	OS	−1.50		20/20		Patching: 4.6 h day^{-1}
J.W. (28.5) (F)	OS	+11.50	136/150	20/30	Manifest OS	Strabismus surgery for LET at age 13.1 years
	OD	Plano		20/20		Patching: 3.0 h day^{-1}
S.D. (7.9) (F)	OS	+15.50	127/176	20/60	None	Strabismus surgery for LXT at age 3.6 years
	OD	Plano		20/20		Patching: 3.6 h day^{-1}
R.R. (5.8) (M)	OD	+14.25	155/183	20/200	None	No other surgery or complications
	OS	Plano		20/25		Patching: 2.5 h day^{-1}
A.T. (12.1) (F)	OS	+17.50	152/245	20/200	Latent OU	Strabismus surgery for LET at age 1.0 years
	OD	Plano		20/20		Patching: 3.6 h day^{-1}
T.A. (16.7) (F)	OD	+17.00	Birth/247	1/200	Latent OS	Strabismus surgery for RET at 5.0 years & RXT at 13.5 years
	OS	−1.00		20/30		Patching: 3.3 h day^{-1}
A.F. (17.8) (F)	OD	+19.25	120/250	20/800	None	Strabismus surgery for RET at age 6.2 years
	OS	Plano		20/25		Patching: 2.6 h day^{-1}
A.M. (19.6) (F)	OD	+11.00	88/313	20/400	Latent OD	Strabismus surgery for RET at age 1.4 years
	OS	Plano		20/20		Patching: 1.6 h day^{-1}

[a] Patients are listed in order of increased deprivation.
[b] Measurement closest to the time of the test. Refractions are spherical equivalents.
[c] OD, right eye; OS, left eye; OU, both eyes; RET, right esotropia; LET, left esotropia; RXT, right exotropia; LXT, left esotropia.

We assumed that any child who had a dense central cataract diagnosed on the first eye exam before 6 months of age had been deprived from birth because it would be unusual to have a dense cataract develop rapidly between birth and 6 months. Consequently, we defined the duration of deprivation as the period extending from birth until the age of first optical correction following surgery to remove the cataract (i.e. the

first time the deprived eye received focused visual input onto the retina). In the present sample, the duration of deprivation ranged from 1.3 to 10.4 months.

All participants received occlusion therapy as a treatment for amblyopia. Occlusion therapy was initiated shortly after the time of the first optical correction and continued through at least 5 years of age (or in the one younger child, until the time of the test). Depending on the ophthalmologist, patients were instructed to patch the non-deprived eye for times ranging from 4 waking h day^{-1} to as much as all but 1 h of waking time day^{-1}. However, because of variation in compliance, the mean amount of patching from the time of the first optical correction until 5.0 years of age ranged from 1.6 to 7.1 waking h day^{-1} (see Lewis et al., 1995 for details of these calculations).

2.2. Apparatus and stimuli

The apparatus and stimuli were identical to those used previously for patients treated for bilateral congenital cataract (Ellemberg et al., 1999b). Briefly, spatial vision was measured with vertical sinusoidal gratings generated on a green phosphor Tektronix 5130 oscilloscope CRT display. The display was 13° wide and 10° high when viewed from a distance of 57 cm. Spatial contrast sensitivity was measured at 0.33, 0.5, 1, 2, 3, 5, 10, and 20 c deg^{-1}. Grating acuity was assessed with a contrast level of 52%. The contrast of the stimuli was defined as the difference between maximum and minimum luminance divided by their sum.

Temporal vision was measured with a spatially unpatterned light display, the luminance of which was varied over time with a sinusoidal function generator. The display was 5° in diameter when viewed from a distance of 57 cm. Temporal contrast sensitivity was measured at 5, 10, 20, and 30 Hz. Critical flicker fusion frequency was assessed at a contrast level of 65%.

The space- and time-average luminances of the test stimuli were 9 cd m^{-2}. Gamma correction was verified by using a Minolta LS-100 photometer. All stimuli were within the range in which contrast was linearly related to the Z-axis voltage (i.e. 52 and 65% for spatial and temporal contrast stimuli, respectively).

2.3. Procedure

The procedure was identical to that reported in Ellemberg et al. (1999b) for patients treated for bilateral congenital cataract. Briefly, participants had one eye patched with 3M Micropore™ tape (half were tested first with the deprived eye and half were tested first with the fellow non-deprived eye) and viewed the display through a 3.5 mm artificial pupil in order to minimize the effects of differences among patients in the shape and size of their pupils. The deprived eye of each patient was corrected optically for the viewing distance by the patient's contact lens and, if necessary, by an additional spectacle lens mounted in a trial frame in front of the eye.

Spatial and temporal thresholds were measured by the method of limits. Spatial contrast sensitivity was assessed at a viewing distance of 57 cm for spatial frequencies ranging from 0.33 to 10 c deg^{-1}, and at twice that distance for spatial frequencies of 20 c deg^{-1}. Three ascending and three descending thresholds were recorded for each spatial frequency, with the ascending thresholds measured first. Participants were asked to indicate when the stimulus just appeared as contrast was increased from subthreshold values — ascending threshold — and to indicate when the stimulus first disappeared as contrast was reduced from suprathreshold levels — descending threshold. The frequencies were tested in a random order. The procedure for testing grating acuity was the same except that participants were moved back to a viewing distance of 228 cm and they were asked to indicate when the stimulus first disappeared as spatial frequency was increased from suprathreshold values, or just reappeared as spatial frequency was decreased from subthreshold values.

Temporal contrast sensitivity was assessed from a viewing distance of 57 cm. Participants were asked to indicate the point when flicker first appeared as temporal contrast was increased from non-visible flicker values. We measured only ascending thresholds because a bright flickering light can cause afterimages that persist after the flicker is no longer visible. Such afterimages during the assessment of a descending threshold would lead to inaccurate estimates of thresholds. Three ascending thresholds were taken for each temporal frequency, with the frequencies tested in a random order.

Critical flicker fusion frequency was also assessed at a viewing distance of 57 cm, but both ascending and descending thresholds were measured, in accordance with the classical literature (De Lange, 1952, 1954). Participants were asked to indicate the point at which the light ceased to flicker as temporal frequency was increased from visible flicker levels, and then to indicate the point at which flicker reappeared as temporal frequency was decreased from non-visible flicker values. Three ascending and three descending thresholds were recorded, with the ascending thresholds always measured first.

Half of the subjects first received the tests for grating acuity and spatial contrast sensitivity, with grating acuity always measured first. The remaining half first received the tests for critical flicker fusion frequency and temporal contrast sensitivity, with critical flicker fusion frequency always measured first. Age-matched normal controls received the same testing and eye order as did the patient with whom they were matched.

2.4. Data analysis

Spatial and temporal contrast sensitivity at each frequency were derived by taking the reciprocal of the geometric mean of the recorded contrast thresholds. For analysis and plotting, the thresholds were log transformed.

The data for each patient are plotted as relative sensitivities, which are defined in the following way:

$$\text{relative sensitivity} = \log \text{patient sensitivity} - \log \text{normal sensitivity}$$

We used pairwise comparisons with Bonferroni corrections to assess differences between the deprived eyes and controls, and between the non-deprived eyes and controls for each of four measures: spatial contrast sensitivity at 0.5 c deg^{-1} (the highest spatial frequency to which all deprived eyes were sensitive), temporal contrast sensitivity at 5 Hz (where losses were greatest), grating acuity, and critical flicker fusion frequency.

We used simple regression analyses to compute the effect of the amount of patching on the same four measures. Because visual outcome can be influenced by the amount of patching and/or the duration of deprivation (Birch et al., 1993,1998; Lewis et al., 1995), the ideal approach would be to do multiple regression analyses with duration of deprivation and amount of patching as independent variables. However, within our patient group, the amount of patching was so highly correlated with the duration of deprivation ($r = 0.83$, $P < 0.0001$), that multiple regression analyses could not separate their independent effects. To minimize the effects of duration of deprivation, we arbitrarily split the patients into those whose deprivation ended before 3.5 months of age ($n = 6$; $M = 2.0$ months; range = 1.3–3.3 months) and those whose deprivation ended later ($n = 9$; $M = 6.7$ months; range 3.9–10.4 months), and re-analyzed the data for these two groups on the same four measures. The division at 3.5 months falls within the range of values chosen in previous studies comparing vision in patients with earlier versus later treatment (e.g. Birch et al., 1993,1998; Maurer & Lewis, 1993).

3. Results

3.1. Deprived eyes: spatial vision

Fig. 1 presents the losses in spatial contrast sensitivity of the deprived and non-deprived eyes from each of the 15 patients treated for unilateral congenital cataract. A value of zero on the ordinate of each panel indicates that the patient's sensitivity is equal to that of the age-matched control, while negative values indicate that the patient's sensitivity was lower than that of the control subject. Fig. 2 shows the loss in grating acuity for the deprived and non-deprived eyes of the 15 patients relative to age-matched normals, plotted as a function of the number of hours per day that the non-deprived eye had been patched.

As shown in Fig. 1A and B, every patient showed losses in spatial contrast sensitivity in the deprived eye that increased with increasing spatial frequency. The deprived eyes of most patients had little if any loss in sensitivity at spatial frequencies below 2 c deg^{-1}. However, half of the patients could not see spatial frequencies that were above 5 c deg^{-1} and those who could showed, on average, a 1.0 log unit reduction at 10 c deg^{-1}. Grating acuity (see Fig. 2) was reduced on average by 0.6 log units. Pairwise comparisons confirmed this pattern of results by showing a significant difference between deprived and control eyes for sensitivity at 5 c deg^{-1} ($t_{28} = 3.2$, $P < 0.002$) and grating acuity $t_{28} = 13.7$, $P < 0.0001$). The amount of patching was not correlated with the size of the deficit at 0.5 c deg^{-1} nor with the deficit in grating acuity ($P = 0.08$).

The results of the simple regression analyses were similar for the six patients with the shortest deprivation (Fig. 1A). Again, the amount of patching was not correlated with the size of the deficit at 0.5 c deg^{-1} nor with the deficit in grating acuity ($P = 0.08$). We note, however, that the one patient in this group whose non-deprived eye was patched only 3.2 h day^{-1} had larger losses than the other five patients, all of whom had patched the non-deprived eye at least 5 h day^{-1}. For the nine patients with longer deprivation (Fig. 1B), the size of the deficit in sensitivity at 0.5 c deg^{-1} was smaller, the more hours per day that the non-deprived eye had been patched ($r = 0.77$, $P = 0.02$).[1] Although the size of the deficit in grating acuity was not correlated with patching ($r = 0.64$, $P = 0.06$), the three patients with the longest deprivation and with little patching of the non-deprived eye (TA, AF, and AM) suffered the largest reductions in grating acuity, reductions of more than 1.0 log units.

3.2. Deprived eyes: temporal vision

As shown in Fig. 3A and B, all patients were able to detect the entire range of temporal frequencies tested. The losses in temporal contrast sensitivity in the deprived eye decreased with increasing temporal frequency. The deprived eyes of most patients had little if any loss in sensitivity at temporal frequencies above 10 Hz. Sensitivity at lower temporal frequencies (5 and 10 Hz) was reduced on average by 0.6 log units. Statistical analyses showed that sensitivity at 5 Hz ($t_{28} = 11.0$, $P < 0.0001$) and critical flicker fusion frequency ($t_{28} = 67.2$, $P < 0.0001$) were significantly worse in deprived eyes than in normal eyes. Sensitivity at 5 Hz was correlated significantly with the amount of patching ($r = 0.51$, $P = 0.05$), and so were the subtle deficits in critical flicker fusion frequency ($r = 0.54$, $P = 0.04$).

In the six patients with the shortest deprivation (Fig. 3a), the losses at low temporal frequencies (5 Hz) were not correlated with the amount of patching ($P > 0.10$). All of these patients had normal critical flicker fusion frequency (see Fig. 4). In contrast, within the group with longer deprivation, the losses in sensitivity at 5 Hz and in critical flicker fusion frequency were smaller, the more hours per day that the non-deprived eye had been patched (5 Hz: $r = 0.66$, $P = 0.05$; cfff: $r = 0.66$, $P = 0.05$).[1]

[1] Because the amount of patching was correlated significantly with the duration of deprivation within this group, we cannot distinguish the independent contributions of these two variables. However, the results make it clear that treatment variables (age of first optical correction and amount of patching) make a difference to the outcome even when treatment has been delayed past 3 months of age.

3.3. Non-deprived eye

Fig. 1 indicates that about half of the non-deprived eyes showed small losses (< 0.14 log units) in sensitivity confined to high spatial frequencies. These losses were not correlated with the number of hours a day that the non-deprived eye had been patched (20 c deg^{-1}, $P > 0.10$) and in fact were largest in two of the three patients with the least patching (AF and AM). Fig. 2 indicates that there were also slight losses in the grating acuity of the non-deprived eye in all patients that averaged 0.13 log units and that were not correlated with patching ($P > 0.10$). Statistical analyses comparing the non-deprived eyes to those of age-match controls confirm this pattern of results by showing a significant difference in acuity ($t_{28} = 4.7$, $P < 0.001$) but not for sensitivity at 5 c deg^{-1} ($P > 0.10$).

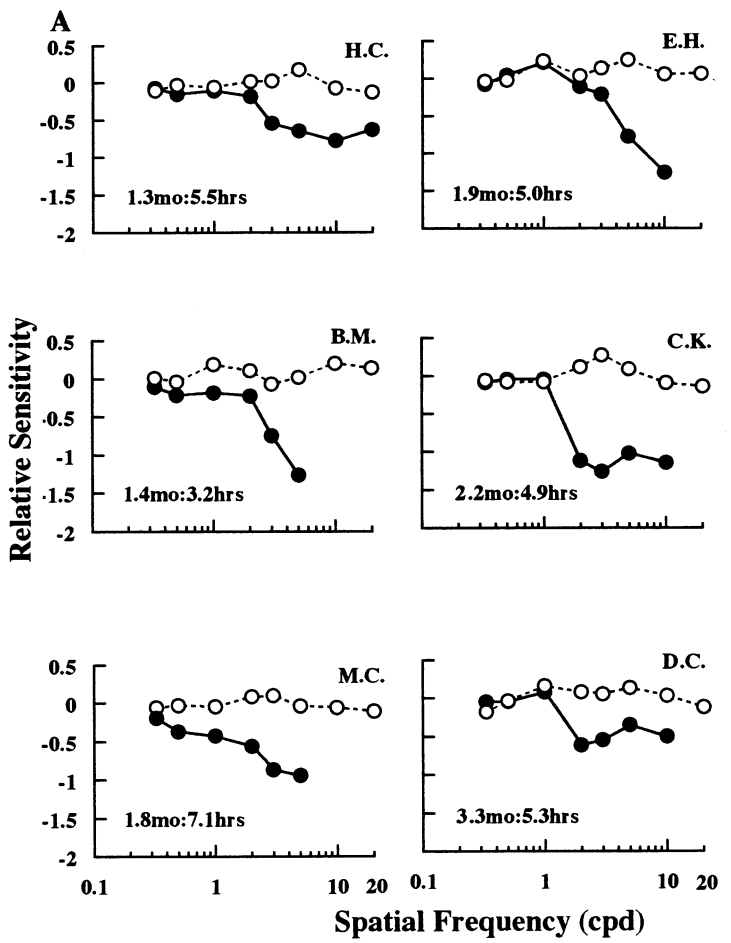

Fig. 1. Relative loss in spatial contrast sensitivity in the deprived eyes (solid circles) and the non-deprived eyes (open circles) of (A) the six patients with the shortest deprivation (< 3.5 months), and (B) the nine patients with longer deprivation (> 3.5 months). Each point represents the log ratio of the patient's sensitivity to the sensitivity of the age-matched normal subject. The numbers in the bottom left corner of each graph indicate the duration of the deprivation in months and the mean number of hours per day of patching from the time of contact lens fitting until age 5 (or the time of test).

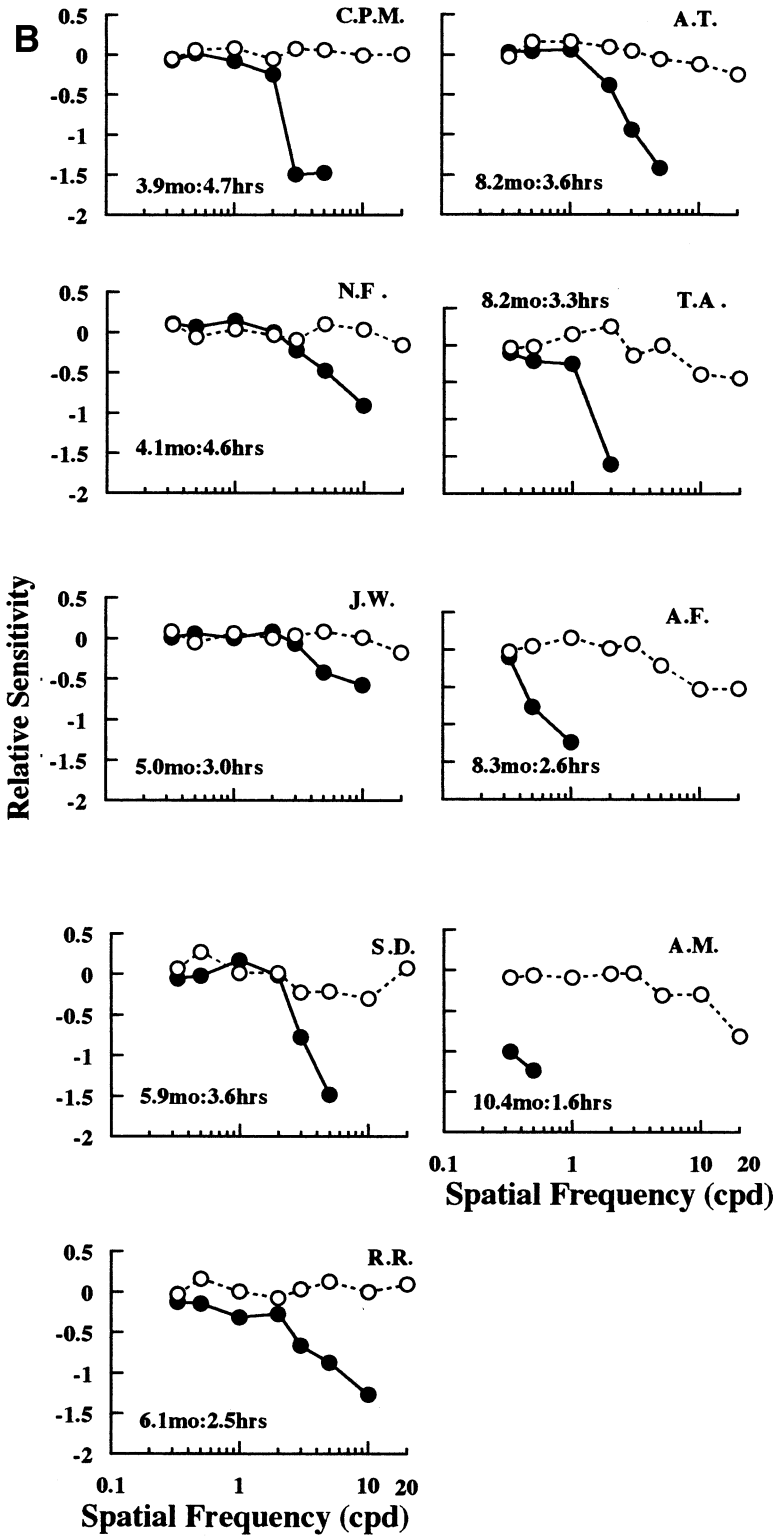

Fig. 1. (*Continued*)

As shown in Figs. 3 and 4, all non-deprived eyes had normal temporal contrast sensitivity and critical flicker fusion frequency. A statistical comparison of sensitivity at 5 Hz and critical flicker fusion frequency confirms that their were no significant differences between non-deprived eyes and controls eyes ($P > 0.10$).

4. Discussion

Monocular deprivation during early infancy resulting from a dense central cataract causes losses in both spatial and temporal vision, with the deficits always greater for spatial vision than for temporal vision. Even in patients with early treatment and aggressive patching of the non-deprived eye, there were losses of about 1.0 log units at high spatial frequencies and losses of 0.5–0.7 log units at low temporal frequencies. The losses at high spatial frequencies are similar to those reported previously in human and non-human primates after short monocular deprivation followed by extensive patching of the non-deprived eye (Tytla et al., 1988; Harwerth, Smith, Crawford, & von Noorden, 1989; Birch et al., 1993,1998). Our study is the first to document that such deprivation also causes deficits in human temporal vision, although the deficits are less severe and occur mainly at low temporal frequencies.

In the patients whose deprivation ended before 3.5 months, we found no correlation between the amount of patching and any of the outcome measures. The lack of a correlation for critical flicker fusion frequency is not surprising since all patients in this group were normal on that measure. Non-significant correlations for the other measures are likely attributable to the fact that only one patient in this group had patched the non-deprived eye less than 5 h day^{-1}. However, it is well documented in the literature that patching is beneficial even after short periods of deprivation (Mayer et al., 1989; Maurer & Lewis, 1993; Lewis et al., 1995).

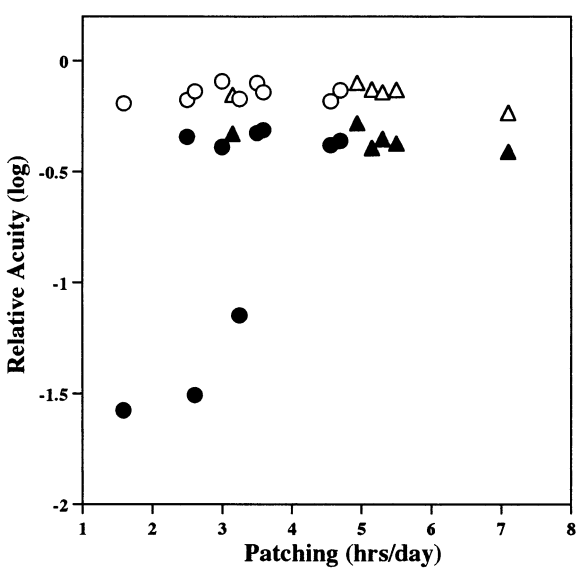

Fig. 2. Relative loss in grating acuity of the deprived eyes (solid symbols) and the non-deprived eyes (open symbols) of patients with earlier (triangles) and later treatment (circles). Each point represents the log ratio of the patient's acuity to the acuity of the age-matched normal subject, plotted as a function of the number of hours per day that the non-deprived eye was patched.

In the patients whose deprivation ended after 3.5 months, we found that the fewer hours the non-deprived eye had been patched, the worse the outcome for spatial sensitivity at 5 c deg^{-1}, temporal sensitivity at 5 Hz, and critical flicker fusion frequency. Although the size of the deficit in grating acuity was not correlated with the amount of patching, the three patients with the longest deprivation and with little patching of the non-deprived eye had the worst grating acuity. These results indicate that even after long periods of deprivation, patching is still beneficial for both spatial and temporal vision.

Because the amount of patching was correlated highly with the duration of deprivation, we could not distinguish the independent contributions of these two variables in the group of patients as a whole. Nonetheless, inspection of Figs. 1–3 indicates the worst outcomes for spatial and temporal contrast sensitivity and acuity in the four patients (AT, TA, AF, and AM) with the longest deprivation (>8 months) and the least patching (<4 h day^{-1}).

Although the patients with longer deprivation had deficits that covered all temporal frequencies and even extended to critical flicker fusion frequency, they showed the same pattern as the patients with shorter deprivation: decreasing deficit with increasing temporal frequency (see Figs. 3 and 4). However, the details of their temporal deficits differ from those in monocularly deprived monkeys (Harwerth et al., 1983b, 1991) and in the only two patients reported previously who had losses in temporal contrast sensitivity that increased with temporal frequency (CT in Manny & Levi, 1982a,b; RC in Hess et al., 1981). These reports may reflect the effect of very long-term monocular deprivation and little occlusion of the non-deprived eye: CT had 18 months of initial deprivation (until the first attempt to optically correct the aphakic eye and initiate patching) followed by later deprivation beginning at 30 months when optical correction was discontinued; RC's aphakic eye was never given an optical correction except for a short attempt with glasses and patching after 5 years of age; Harwerth's monkeys suffered continuing deprivation from uncorrected refractive errors after the initial period of lid suture, which was not followed by occlusion of the non-deprived eye. These comparisons suggest that the longer the deprivation, the more likely that the higher temporal frequencies will be affected. Very long deprivation might cause the greatest deficit at high temporal frequencies because it damages not only cortical cells (see below), but also leads to retinal degeneration (Von Noorden, Crawford, & Middleditch, 1977).

In a previous study using the same methods (Ellemberg et al., 1999b), we found that humans treated for bilateral congenital cataract after 1–9 months of depri-

vation also show reductions in spatial and temporal vision, with the deficits always greater for spatial than for temporal vision. A comparison between studies indicates that the losses in spatial and in temporal vision after binocular deprivation were similar to those shown by most patients treated for monocular deprivation. However, our four patients with the longest deprivation and least patching have much worse outcomes than any of the patients treated for binocular deprivation. Our findings agree with those of Birch et al. (1998), who showed that children who received later treatment of their unilateral congenital cataract (> 3.0 months) had significantly larger deficits in spatial vision than children who received early treatment of unilateral and bilateral congenital cataract (< 2.0 months), with both of these latter groups having similarly small deficits.

Our findings are consistent with the hypothesis that the effects of deprivation are related to the normal pattern of development such that the aspects of vision that are slowest to mature are the ones that are most affected by deprivation (Maurer & Lewis, 1993). For example, acuity and sensitivity at high spatial and low temporal frequencies develop more gradually and mature later than do critical flicker fusion frequency and sensitivity at high temporal and low spatial frequencies both during infancy (Atkinson, Braddick, & Moar, 1977; Banks & Salapatek, 1978, 1981; Regal, 1981) and childhood (Ellemberg et al., 1999a). Both after monocular (this study) and after binocular deprivation (Ellemberg et al., 1999b), it is these slowly developing aspects of spatial and temporal vision that are most affected by deprivation.

We attribute the losses in spatial and temporal vision to early visual deprivation caused by a dense central cataract preceding the aphakia (the postsurgical absence of a natural crystalline lens) and not to aphakia per se. Ellemberg et al. (1999b) used the identical procedure to test the vision of two patients who had had a normal visual history until they developed a dense central cataract in one eye as a result of an injury after 11 years of age. Like the patients in this study, they were fitted with a contact lens following removal of the cataract. Unlike the patients in this study, their spatial and temporal vision did not differ from those of age-matched controls.

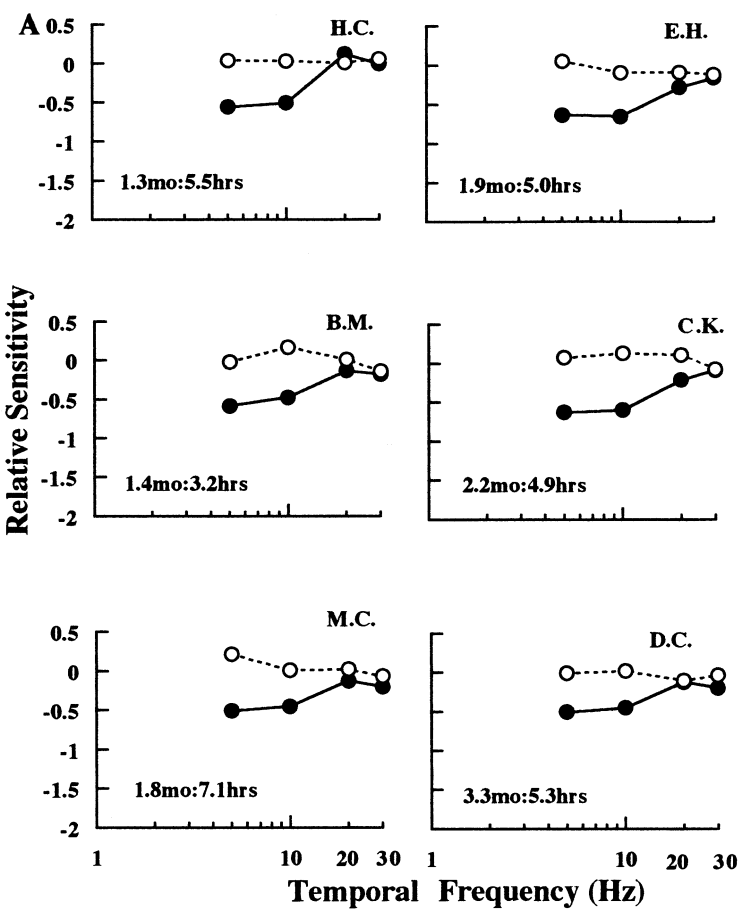

Fig. 3. Relative loss in temporal contrast sensitivity of the deprived eyes (solid circles) and the non-deprived eyes (open circles) of (A) the six patients with the shortest deprivation (< 3.5 months) and (B) the nine patients with longer deprivation (> 3.5 months). Each point represents the log ratio of the patient's sensitivity to the sensitivity of the age-matched normal subject. Other details as in Fig. 1.

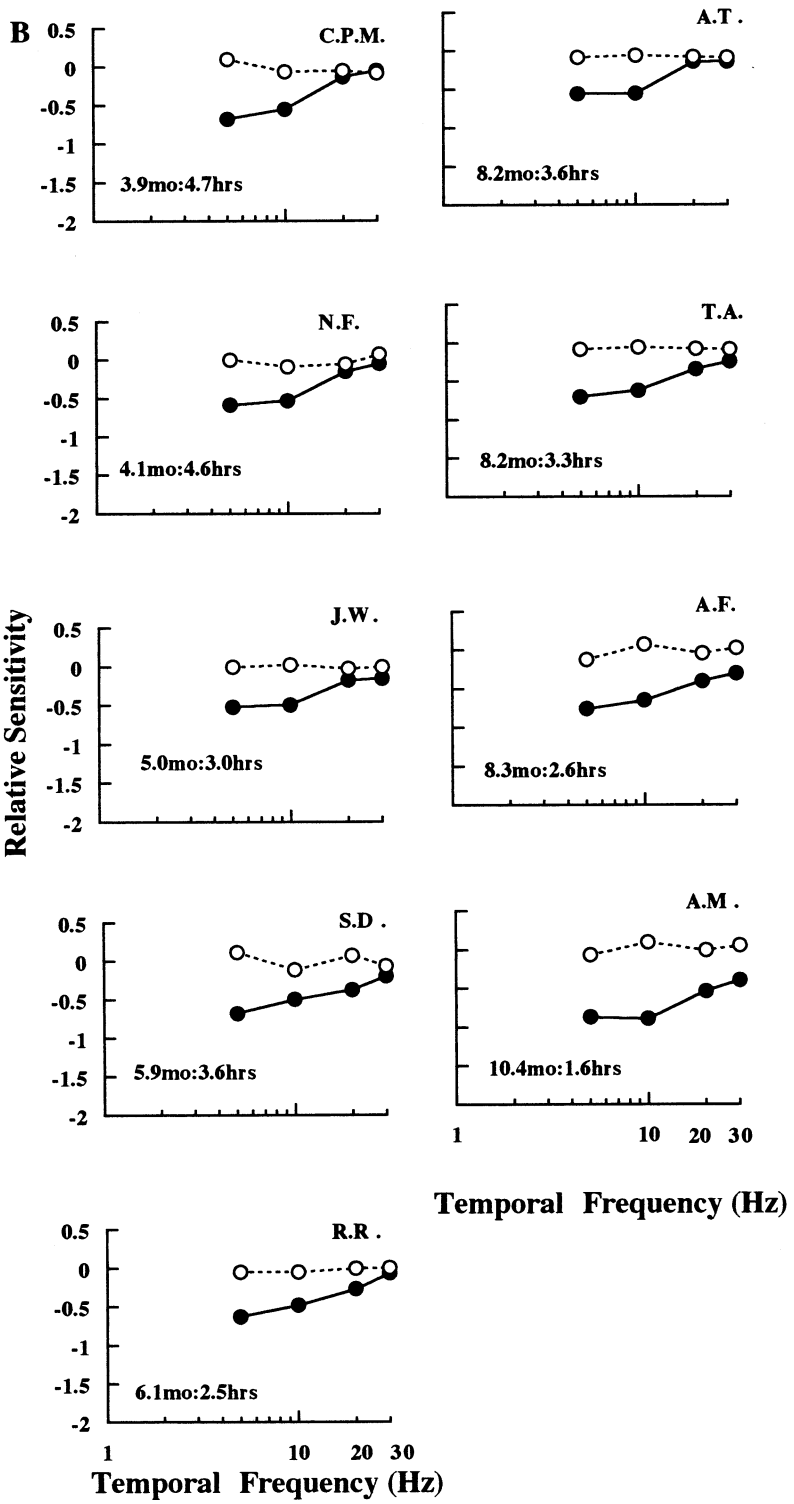

Fig. 3. (*Continued*)

Associated disorders like horizontal nystagmus and strabismus present in many of our patients are also unlikely to be responsible for the losses in spatial and temporal vision. Two of the patients had no strabismus and no nystagmus (EH & RR), and three other patients had no nystagmus (see Table 1); yet their pattern of deficits for both spatial and temporal vision was similar to that of our patients with strabismus and/or nystagmus. Further, losses in patients with strabismic amblyopia are typically less severe than those shown by our patients (Hess & Howell, 1977). Horizontal nystagmus found in many of our patients could possibly blur the

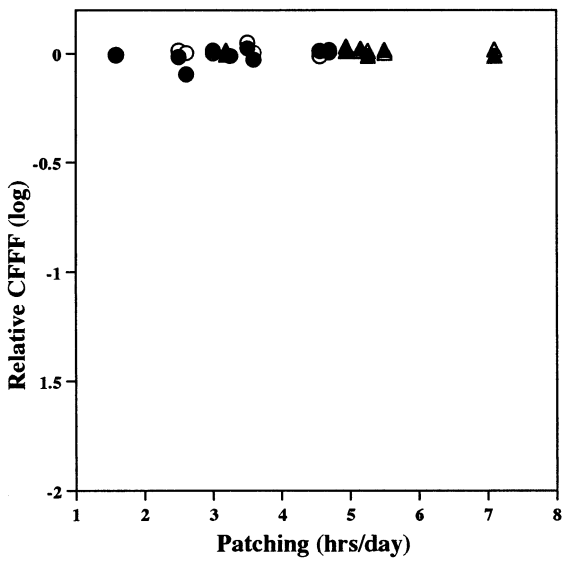

Fig. 4. Relative loss in critical flicker fusion frequency of the deprived eyes (solid symbols) and the non-deprived eyes (open symbols) of patients with earlier (triangles) and later treatment (circles). Each point represents the log ratio of the patient's critical flicker fusion frequency to the critical flicker fusion frequency of the age-matched normal subject, plotted as a function of the number of hours per day that the non-deprived eye was patched.

high spatial frequencies of gratings oriented orthogonally to its direction. However, nystagmus is unlikely to account for the losses at low spatial frequencies found in some patients. Nor can it account for the losses in temporal contrast sensitivity because the temporal modulation always stimulated all parts of the retina. Moreover, it may not contribute to the losses even at high spatial frequencies because Higgins, Daugman, and Mansfield (1982) found that stabilizing a grating on the retina of an amblyope with nystagmus did not improve sensitivity, and that jiggling a grating did not decrease sensitivity of a normal eye. In summary, it seems that the pattern of losses in spatial and temporal vision resulted from early pattern deprivation and not from associated strabismus or nystagmus.

Other associated disorders like microcornea and shortened axial length of the deprived eyes are also unlikely to be responsible for the losses in spatial and temporal vision. The seven patients with microcornea and/or shortened axial length (CK, CPM, NF, AT, TA, AF, & AM) had a similar pattern of deficits for both spatial and temporal vision as did the eight patients with normal corneal diameter and axial length, including two who also had no strabismus and no nystagmus (EH & RR). In addition, Griener and associates (Griener, Dahan, & Lambert, 1999) found no systematic relation between differences in axial length and differences in acuity between the two eyes of patients treated for unilateral cataract. Finally, each eye in our sample was tested with an optical correction that focused input on the retina and hence compensated for any abnormality in axial length or corneal curvature at the time of the test.

4.1. Mechanisms of monocular deprivation

Losses in spatial and temporal vision are likely caused at the level of the striate cortex and beyond because monocular deprivation in monkeys resulting from unilateral lid-suture causes no change in photoreceptor topography (Clark, Hendrickson, & Curcio, 1988), electroretinograms (Crawford, Blake, Cool, & von Noorden, 1975), or the physiological properties of LGN neurons (Blakemore & Vital-Durand, 1986). In contrast, abnormally few striate cortex neurons respond to stimulation of the deprived eye (LeVay, Wiesel, & Hubel, 1980; Horton & Hocking, 1998; Crawford, Pesch, von Noorden, Harwerth, & Smith, 1991). However, occlusion of the monkey's non-deprived eye through reverse suturing increases the proportion of striate neurons driven by the deprived eye (Blakemore, Garey, & Vital-Durand, 1978; LeVay et al., 1980; Swindale, Vital-Durand, & Blakemore, 1981; Crawford, de Faber, Harwerth, Smith, & von Noorden, 1989). These cortical changes in response to occlusion could account for the significant correlation between both spatial and temporal sensitivity and the amount of patching. The competitive interaction in striate cortex between the deprived and non-deprived eyes may reflect competition between geniculocortical afferents from each eye for neurotrophic support in the striate cortex (e.g. Carmignoto, Canella, Candeo, Comelli, & Maffei, 1993; but see Caluske, Kim, Castren, Thoenen, & Singer, 1996) and/or may be the result of desynchronization between the pre-synaptic activity driven by the deprived eye and the post-synaptic activity driven by the non-deprived eye (Hata & Stryker, 1994).

Finally, the slight reduction in the grating acuity of the non-deprived eye is likely of cortical origin. Both the present study and our previous study of a similar cohort (Lewis, Maurer, Tytla, Bowering, & Brent, 1992) found no relation between reductions in grating acuity and the amount of time that the non-deprived eye had been patched. In fact, in the current study the reductions were greatest in the patients with the least patching. Since the non-deprived eyes appeared entirely normal on ophthalmological examination (except for minimal refractive errors and some incidences of nystagmus — see Table 1), the most likely explanation is that amblyopia is central in origin and therefore affects both eyes.

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