

# Multiple Short Daily Periods of Normal Binocular Vision Preserve Stereopsis in Strabismus

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**PURPOSE.** Infantile strabismus impedes the development of stereopsis. In optically strabismic monkeys, 2 continuous hours of normal binocular vision per day has been shown to preserve near-normal stereopsis. In this study, we investigated whether, as in learning, multiple shorter periods of intervention would further boost performance.

**METHODS.** To simulate infantile esotropia, infant monkeys were reared with 30 prism diopters base-in starting at 4 weeks of age. Daily periods of normal binocular vision were provided by replacing prisms with plano lenses. Altogether, 14 monkeys were prism reared: 2 with continuous prism, 2 with 2 continuous hours of normal binocular vision per day, 6 with 2 noncontinuous hours, and 4 with 1 noncontinuous hour of binocular vision each day. Seven normally reared monkeys provided control data. Behavioral methods were employed to measure spatial contrast sensitivity, eye alignment, and stereopsis.

**RESULTS.** One monkey reared with continuous prism had poor stereopsis, and the other had no stereopsis. Ten of the 12 monkeys reared with periods of normal binocular vision had stereopsis, and those with longer and more continuous periods of binocular vision had stereopsis approaching that of normally reared monkeys.

**CONCLUSIONS.** During early development, multiple short periods of binocular vision were effective in preserving clinically significant stereopsis in monkeys. These results suggest that by providing relatively short multiple daily intervention periods, stereopsis may be preserved in strabismic human children.

Keywords: stereopsis, development, strabismus, monkey

Stereopsis is the primary benefit of having frontally positioned eyes and simultaneous binocular single vision. Normal stereopsis is the culmination of supporting visual functions in that it requires that each eye have good spatial vision, motor coordination maintains bifoveal fixation, sensory fusion combines right and left eye images into a stable single percept, and disparity-tuned mechanisms are sensitive to crossed and uncrossed disparities. Normal humans and monkeys are capable of extracting accurate relative depth information from horizontal retinal image disparities as small as a few seconds of arc.<sup>1-3</sup>

Humans and monkeys are born with rudimentary binocular visual function. To mature, normal binocular visual experience is required during the early critical period of visual development to reinforce neural connections relaying corresponding visual information from the two eyes to the visual cortex. Strabismus can interfere with normal binocular visual development, especially if it occurs during the critical period and is constant. By interrupting the constancy of the abnormal strabismic sensory experience with short durations of normal binocular vision, stereopsis can be preserved in laboratory animals.<sup>4,5</sup>

Two lines of evidence demonstrate that very young infants have the neural mechanisms required to support stereopsis. Single-cell electrophysiologic recordings in the primary visual cortex of a 6-day-old monkey revealed that the response amplitude of many neurons varied systemati-

cally as a function of interocular spatial disparity. In recording from many cells in the cortex, it was found that infant monkeys have the same proportion of disparity-sensitive cells as adults.<sup>6</sup> Normal human infants can behaviorally respond to binocular disparity starting at between 3 and 5 months of age,<sup>7</sup> and prism-corrected infantile esotropes were also able to distinguish stereo from nonstereo targets at this same age.<sup>8</sup> Although these esotropes subsequently lost disparity sensitivity, these results show that they possessed the neurologic mechanisms required to support stereopsis prior to succumbing to the disruptive effects of strabismus.

Infantile esotropia is one of the most common forms of strabismus in infants younger than 6 months of age.<sup>9,10</sup> While smaller deviations may spontaneously resolve, constant large-angle (20–40 prism diopter (pd)) deviations do not.<sup>11,12</sup> Currently, the standard time for surgical alignment is 11 to 18 months of age,<sup>10</sup> but there is a growing opinion that alignment surgery should be performed as early as is possible,<sup>10,13,14</sup> specifically to limit the duration of constant strabismus.<sup>15</sup> Historically, very early surgery performed prior to 6 months of age resulted in a vanishingly small number of cases that appeared to have bifoveal fixation and functionally normal stereopsis,<sup>15-18</sup> but most were resigned to subnormal binocular vision (microtropia or monofixation syndrome) functionally identical to infants who were surgically aligned up to 2 years of age.<sup>14,18-25</sup> With surgery, eye alignment is cosmetically acceptable, being within 8 prism



diopeters of orthotropia.<sup>26</sup> Because of peripheral fusion, there are normal motor fusional ranges and gross stereopsis but not fine stereopsis, owing to a small suppression scotoma that encompasses the fovea and the diplopia point of the turned eye.<sup>21</sup>

The disappointing results observed with very early surgery have prompted vision scientists to try to understand the cause of infantile esotropia and to investigate novel approaches to capitalize on early innate binocular visual potential. Second only to occurrence within the critical period, constancy of strabismus appears to present the most significant risk to the developing binocular visual mechanisms. Laboratory investigations in which the constancy of strabismus was interrupted with intervals of normal binocular vision on a daily basis have shown that in monkeys<sup>4</sup> and kittens,<sup>5</sup> stereopsis can be preserved. In monkeys, 2 hours per day of normal binocular vision preserved near-normal stereopsis despite 10 hours per day of otherwise constant strabismus simulated over a duration of 4 to 6 weeks. In kittens, 2 hours per day of normal binocular vision successfully prevented amblyopia, but only one of three animals demonstrated better task performance based on real depth with two eyes as opposed to with just one eye.

Our goal in this investigation was to determine if there is a minimum threshold requirement of 2 continuous hours of normal visual experience for monkeys to retain stereopsis. Following from this, we investigated whether distributing the duration of normal visual experience over shorter multiple periods would improve binocular visual outcome. The phenomenon of the “spacing effect” from learning literature, in which multiple shorter durations were superior to a single longer-duration practice session resulted in superior retention of the knowledge or skill, would support this result.<sup>27–29</sup> The superiority of multiple short periods of normal visual experience compared to fewer longer durations has also been previously demonstrated in the recovery from form deprivation amblyopia in monkeys<sup>30</sup> and kittens.<sup>31</sup> The impetus for investigating the temporal integration properties of the development of binocular visual mechanisms in this way is that for the results gleaned from animals to be practical for application to human infants, the temperament of infants must be taken into account. Parents need to know if it is worth the effort to try to keep prism spectacles on the infant, for example, if it is only possible for short periods during the day, to preserve binocular function until the eyes are surgically aligned.

## METHODS

### Subjects

Data are presented for 21 rhesus monkeys (*Macaca mulatta*). Infant monkeys were obtained between 1 and 3 weeks of age and reared in the university primate nursery, which was kept on a 12-hour light/12-hour dark day/night schedule. During the dark cycle, all lights in the nursery were turned off, but because there may have been some light penetrating from under the door to the lighted hallway, the darkness in the nursery was unlikely to be total darkness. All rearing and experimental procedures were approved by the University of Houston’s Institutional Animal Care and Use Committee and were in compliance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research.

Optical strabismus was created by mounting 15 diopter prisms oriented base-in in front of each eye (30 Base In (BI) total) in a lightweight helmet, as previously described.<sup>32–34</sup> Fourteen monkeys were prism reared from 3 to 4 weeks of age for durations of either 4 or 6 weeks (Table). The prism-rearing regimen was purposefully delayed because visual manipulations like optical strabismus are less likely to result in an overt eye turn if initiated after age 3 weeks.<sup>35–37</sup> Following prism rearing, helmets were removed and monkeys were allowed unrestricted normal binocular vision.

Two monkeys wore the prisms continuously (CP-1 and CP-2). Twelve monkeys wore the prisms, but eight were allowed 2 hours of normal binocular vision each day by replacing the prisms with clear plano lenses. Of these, two monkeys had one period of 2 continuous hours without the prisms each day (C2hr-1 and C2hr-2), four monkeys had two periods of 1 hour without the prisms (2hr-1 to 2hr-4), and two monkeys had four periods of a half-hour without the prisms (4half-1 and 4half-2). In addition, four monkeys were allowed 1 hour of normal binocular vision each day, but that 1 hour was divided into four 15-minute periods (4qtr-1 to 4qtr-4). The periods of normal binocular vision were equally distributed throughout the 12 hours of lights-on (7 AM to 7 PM) in the infant nursery. The four periods of normal binocular vision were started at 9 AM, 11 AM, 1 PM, and 3 PM, and the two periods of normal binocular vision were started at 11 AM and 3 PM each day. Helmets in which the prisms were mounted were not removed overnight. Seven normally reared monkeys provided control data (NR-1 to NR-7).

Data from some of these monkeys have previously been reported.<sup>4</sup>

### Apparatus and Visual Stimuli

Behavioral training and testing were initiated at 2 years of age, so that monkeys had experienced at least 1 year and 9 months of normal vision since prism rearing, ensuring that all deficits observed were permanent. For the daily experimental sessions, monkeys were seated in a primate chair fitted with a response lever on the waist plate and a drink spout on the neck plate. Their optimal spectacle correction, determined for each eye by retinoscopy and refined behaviorally,<sup>35</sup> was mounted in the facemask at about a 14-mm vertex distance (Table).

### Spatial Contrast Sensitivity

Stereopsis can be deficient because monocular spatial vision is degraded. In order to elucidate exactly why stereopsis might be reduced in our subjects, monocular spatial contrast sensitivity functions were determined for each monkey, using the same apparatus and operant procedures as in previous investigations.<sup>30,35,37–39</sup> Briefly, the detection stimuli were Gabor patches of vertical sinusoidal gratings windowed by a 2-degree Gaussian envelope, presented on an 11 × 14-degree video monitor with a space-averaged luminance of 60 cd/m<sup>2</sup>. The stimulus contrast was Michelson contrast (difference between the maximum and minimum luminances of the grating divided by the sum of the maximum and minimum luminances).

In the temporal interval detection paradigm, monkeys pressed down on a lever to initiate a trial and then released the lever within 500 ms following stimulus presentation to score a “hit.” The stimuli were presented with equal probability between 250 and 6000 ms after the initial lever

**TABLE.** The Following Data are Listed for Each Monkey Included in this Investigation: Each Subject's Specific Symbol in all Figures and Name in the Text, the Number and Length of Periods Without the Prism Each Day and The Duration of Prism Rearing in Weeks, the Refractive Error of the Right Eye and Left Eye in Diopters, the Cutoff Spatial Frequency for the Right Eye and Left Eye Derived from the Fitted Monocular sPatial Contrast Sensitivity Functions in Cycles Per Degree, the Associated Phoria from the Forced Vergence Fixation Disparity Functions in Prism Diopters Base in (BI) or Base Out (BO). For Local Stereopsis, the Best Measured Threshold in Arcminutes and the Spatial Frequency of the Gabor Carrier Grating at Best Threshold, and for Global Stereopsis the Best Measured Threshold in Arcminutes.

subject		prism rearing		refractive error		contrast sensitivity		associated phoria		local stereopsis		global stereopsis	
symbol	name	treatment	duration	right eye: left eye		cutoff spatial frequency		Base in:	Base out	best	sf	best	
		daily	weeks	diopters		cy/deg		prism diopters		arcmin	cy/deg	arcmin	
□	NR-1	normal		OD PL		30.0		2 BI		0.18	4.00	~	
				OS PL		24.9							
◇	NR-2	normal		OD -0.50D		14.0		~		0.35	2.82	~	
				OS -0.50D		15.9							
○	NR-3	normal		OD PL		23.1		OPD		0.11	5.64	0.12	
				OS PL		21.5							
△	NR-4	normal		OD +0.50D		25.3		~		0.20	5.64	~	
				OS +0.50D		22.6							
⬡	NR-5	normal		OD PL		17.2		4BO		0.19	5.64	0.15	
				OS PL		17.8							
▽	NR-6	normal		OD PL		16.6		6 BI		0.14	2.00	0.20	
				OS PL		18.8							
☆	NR-7	normal		OD +1.00D		10.8		11 BI		3.40	5.64	6.74	
				OS +6.00D		10.7							
⬢	CP-1	no breaks	4 weeks	OD -1.50D		23.3		2 BI		16.00	2.82	3.30	
				OS -1.00D		20.6							
▼	CP-2	no breaks	6 weeks	OD +11.00D		3.9		2 BI		~	~	~	
				OS +11.00D		5.7							
■	C2hr-1	2 hours	4 weeks	OD PL		25.7		2 BI		0.43	1.41	0.44	
				OS PL		26.1							
◆	C2hr-2	2 hours	6 weeks	OD +1.00D		29.1		4 BI		0.64	2.00	0.85	
				OS +1.00D		26.1							
▲	2hr-1	2x60min	6 weeks	OD PL		17.8		OPD		0.49	1.00	0.21	
				OS PL		19.8							
✖	2hr-2	2x60min	6 weeks	OD -1.00D		17.0		5BO		0.54	4.00	0.34	
				OS PL		19.3							
●	2hr-3	2x60min	4 weeks	OD +1.00D		22.6		2BO		0.54	2.82	0.49	
				OS +1.00D		21.7							
+	2hr-4	2x60min	4 weeks	OD PL		17.9		12 BO		1.38	1.00	0.66	
				OS -1.00D		17.3							
▼	4half-1	4x30min	4 weeks	OD +1.00D		23.2		9BO		3.75	2.00	2.57	
				OS PL		4.8							
★	4half-2	4x30min	6 weeks	OD -1.00D		11.4		5BO		~	~	~	
				OS PL		23.1							
●	4qtr-1	4x15min	6 weeks	OD +1.00D		10.8		3BO		0.52	5.64	0.26	
				OS +1.00D		9.7							
▲	4qtr-2	4x15min	6 weeks	OD PL		16.5		4BO		1.26	2.82	0.66	
				OS PL		17.7							
▼	4qtr-3	4x15min	6 weeks	OD PL		13.0		4BO		1.65	5.64	2.84	
				OS PL		11.2							
★	4qtr-4	4x15min	6 weeks	OD -2.00D		17.2		~		~	~	~	
				OS -6.00D		10.5							

press. Data were collected using an adaptive decreasing-contrast staircase, in which each hit was followed by a 0.1 log unit reduction in contrast, and two consecutive misses were followed by a 0.6 log unit increase in contrast. This one-down/two-up strategy caused the staircase reversals to converge to a contrast where the probability of a hit was 29%, and this contrast was taken as the threshold. Contrast

detection thresholds were measured as a function of grating spatial frequency from 0.25 to 16 cycles (cy)/deg in 0.15 log unit steps.

Contrast sensitivity functions were generated from the geometric means of a minimum of 30 threshold measures at each spatial frequency. Data from each eye were fitted with the following double exponential function using an iterative

routine that minimized the sum of squared errors<sup>40</sup>:

$$\text{Contrast sensitivity} = (k_s(sf * kf)^{al}) \exp(-ab * sf * kf)$$

where  $sf$  is the spatial frequency;  $al$  and  $ab$  are parameters that reflect the slopes of the low and high spatial frequency portions of the function, respectively; and  $ks$  and  $kf$  are proportional to the peak contrast sensitivity and the optimum spatial frequency, respectively. High spatial frequency cutoffs were estimated for each eye of each monkey as the spatial frequency corresponding to a sensitivity of 1.0 (Table).

### Fixation Disparity and Interocular Alignment

Stereopsis can also be degraded by strabismus. To investigate eye alignment, forced-vergence fixation disparity functions were generated for each monkey. Procedurally, dichoptic Vernier alignment measures were taken for line stimuli presented against a background that promoted fusion.<sup>3,41</sup> The physical offset of the dichoptically viewed line stimuli at perceptual alignment (fixation disparity) was determined over a range of prism powers (forced vergence). The plot of prism power versus fixation disparity showed how accurate motor fusion was relative to the vergence demand, as well as the prism power that reduced dichoptic vergence error to zero (associated phoria).<sup>42</sup> Monkeys with associated phorias were tested for stereopsis with the corrective prism in place (Table).

### Local and Global Stereopsis

Stimulus generation and the behavioral paradigm have been described previously.<sup>3,4,39</sup> In brief, stereoscopic stimuli were generated by computer graphics (VSG 2/3; Cambridge Research Systems, Cambridge, UK) and dichoptically viewed through liquid-crystal shutters (model LV 100P; DisplayTech, Inc., Longmont, CO, USA) synchronized to the video frame rate of the display. The top reference pattern was presented with no horizontal disparity and separated from the bottom test pattern by a gap of 2 arcmin (local stereo) or 8 arcmin (global stereo).

Local stereopsis was evaluated with one-dimensional Gabor patches that were windowed by a Gaussian along the horizontal aspect only, leaving the top and bottom edges sharp. Four grating cycles were presented at each spatial frequency ranging from 0.25 to 16 cy/deg in half-octave steps.<sup>43</sup> To test global stereopsis, full-density bands of dynamic random dots that spanned the width of the monitor were used. Dots were either black or white, and when there was 100% correlation, the black and white dots in the right eye image matched the polarity of dots in the left eye image. At 50% correlation, half of the dots were forced to match, and the remaining half of the dots were left free to vary randomly. Disparity threshold was measured for percent correlation of dot polarity from 100% to 10% in half-octave steps.

In the go/no-go paradigm, the monkey pressed down on a lever to initiate a trial. When the bottom test stimulus was presented in crossed disparity and appeared closer than the top reference, the monkey released the lever; when the bottom test stimulus was presented in uncrossed disparity and looked farther than the top reference, the monkey held the lever down through the trial. During a daily experimental session, a single Gabor carrier grating spatial frequency

or a single random dot percent correlation was tested. The method of constant stimuli was used in which the bottom test pattern was presented with one of five crossed or uncrossed disparities that were equally distributed along a continuum. The “percent nearer” response was plotted against the continuum of disparities presented and fit with a logistic function. The disparity threshold was taken as half of the disparity range between the 25% and 75% nearer response (intraquartile range),<sup>44</sup> thereby reflecting the slope of the psychometric function or how fast sensitivity changes. The data presented are the means and standard deviations of at least three threshold determinations. Data for global stereopsis were fit with the linear regression function on SigmaPlot software (Systat Software Inc. San Jose, CA, USA)(Windows Version 10.0). To confirm that responses were based on binocular disparity, performance was measured with one eye occluded and found to be at chance.

## RESULTS

### Refractive Error

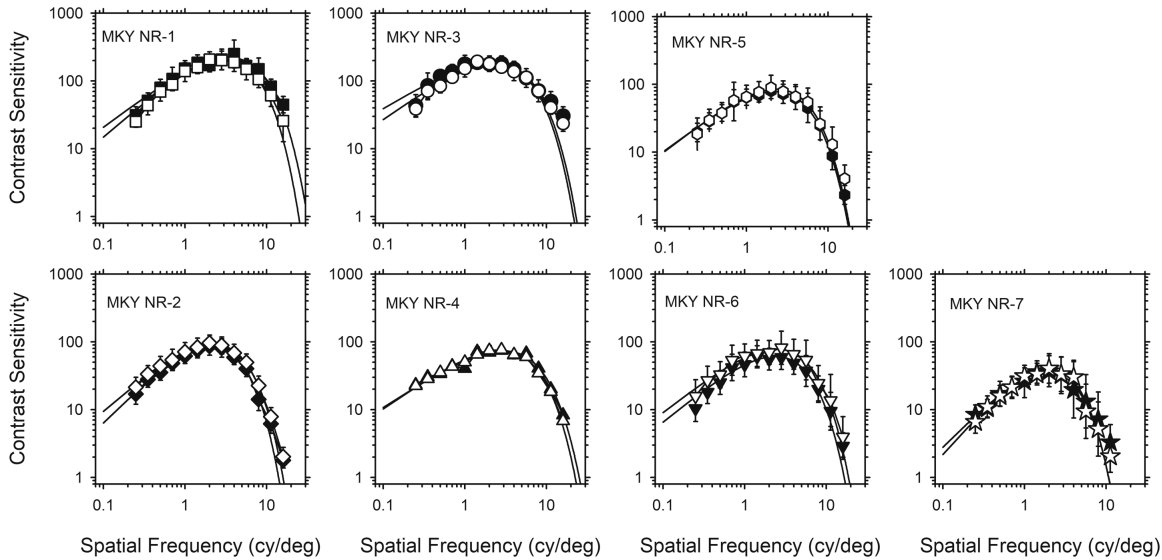
The refractive error of each eye of each monkey was determined at the beginning of behavioral training and testing when the animals were 2 years old (Table). Monkeys had refractive errors that are within the normal range<sup>45</sup> and similar in the two eyes, except for normally reared monkey NR-7 (OD +1.00D, OS +6.00D), monkey CP-2 (+11.00 OU), and monkey 4qtr-4 (OD -2.00D, OS -6.00D). Strabismus does influence refractive error development,<sup>46</sup> and it is likely that the strabismic visual experience of prism rearing contributed to the anisometropia exhibited by monkey 4qtr-4. Monkey NR-7 had a similarly large difference in the refractive errors between her two eyes, but she was normally reared. The data from both monkeys 4qtr-4 and NR-7 were included in the study because of the differences in their visual performance despite similar anisometropias. Monkey CP-2, who was a high bilateral hyperope, was also retained because his refractive error and visual capabilities were likely the consequence of his abnormal binocular visual experience.

### Spatial Contrast Sensitivity

High spatial frequency cutoffs of the spatial contrast sensitivity functions represent grating acuity and are listed for each eye of every monkey in the Table. The spatial contrast sensitivity functions for the normally reared monkeys were alike in that the curves for each of the two eyes were well matched and were of the characteristic bandpass shape (Fig. 1) with normal high spatial frequency cutoffs (average =  $20.6 \pm 4.96$  cy/deg). The exception was monkey NR-7, who showed high spatial frequency cutoffs that were bilaterally lower (OD 10.8; OS 10.7 cy/deg) than those of the other normally reared monkeys. Monkey NR-7 was normally reared but had naturally occurring anisometropia (OD +1.00D, OS +6.00D), which might have been expected to result in unilateral amblyopia of her more hyperopic left eye. Her data were not included in any averages of normal monkey's data.

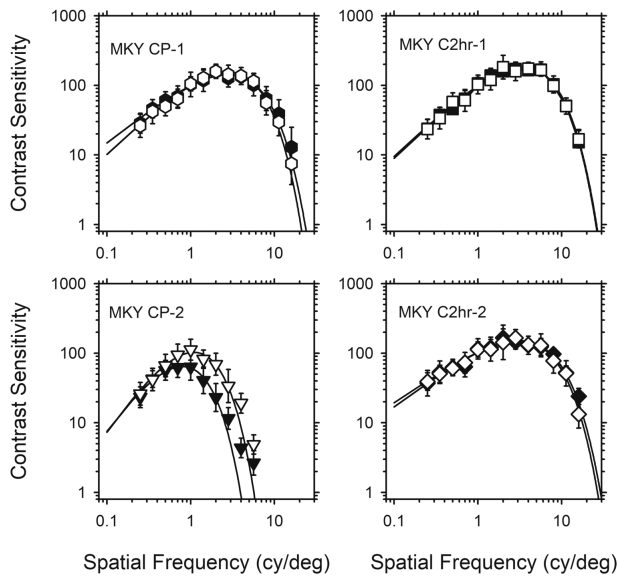
Figure 2 shows the contrast sensitivity functions for the two monkeys who wore the prism continuously (CP-1 and CP-2) and for the two monkeys who were allowed one continuous 2-hour period of normal binocular vision each

Normally Reared Monkeys



**FIGURE 1.** The inverse of the average threshold contrast for each eye was plotted as a function of the grating spatial frequency to generate monocular spatial contrast sensitivity functions. *Open symbols*: right eye sensitivities; *filled symbols*: left eye sensitivities. *Error bars*: standard deviations; *lines*: best-fitting double exponential functions. Where contrast sensitivity is equal to 1 indicates the high spatial frequency cutoff, which is a measure of detection visual acuity. Normally reared monkeys.

Continuous Prism & 2 Continuous Hours BV/Day



**FIGURE 2.** Monocular spatial contrast sensitivity functions for two monkeys reared with continuous prism (CP-1 and CP-2) and for two monkeys reared with 2 continuous hours of normal binocular vision per day (C2hr-1 and C2hr-2). See [Figure 1](#) for details.

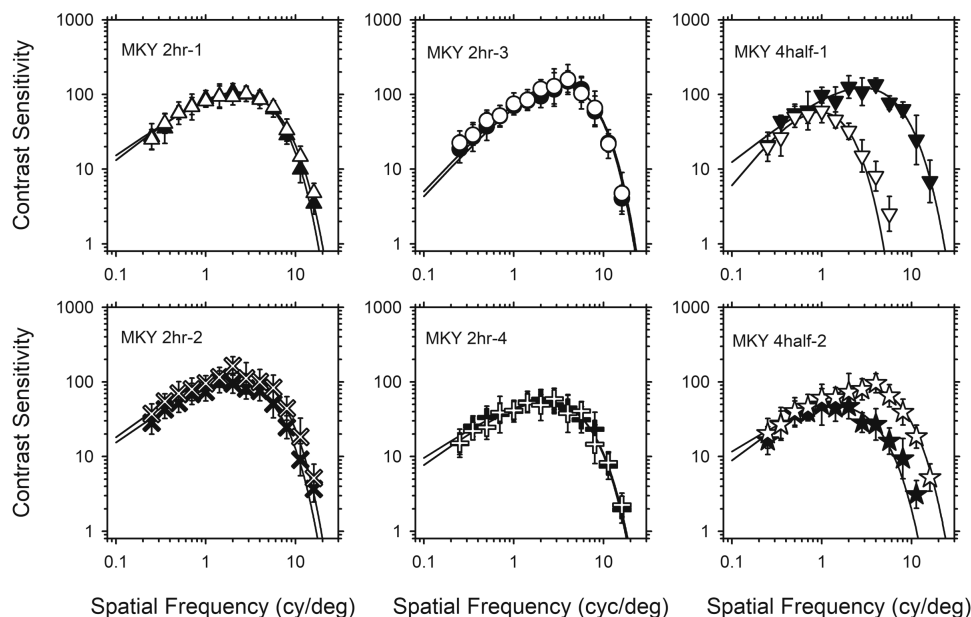
day (C2hr-1 and C2hr-2). In this group, the functions for monkeys CP-1, C2hr-1, and C2hr-2 were similar in shape to those of normally reared monkeys, and the cutoff spatial frequencies were actually higher than the average for normal monkeys (average =  $25.2 \pm 2.89$  cy/deg). Monkey CP-2 had contrast sensitivity functions with normal peak sensitivity but reduced high spatial frequency cutoffs (OD 3.9, OS

5.7 cy/deg), consistent with his bilateral high refractive error (OD +11.00D, OS +11.00D).

[Figure 3](#) shows contrast sensitivity functions for the monkeys who had 2 nonconsecutive hours of normal binocular vision per day. All four who had two periods of 1 hour (2hr-1 to 2hr-4) showed contrast sensitivity functions similar to those of normal monkeys and normal high-frequency cutoffs (average =  $19.2 \pm 2.08$  cy/deg). Both monkeys who had four periods of a half-hour of normal binocular vision each day (4half-1 and 4half-2) showed significant monocular amblyopia in that the function for the amblyopic eye was truncated over the upper range of spatial frequencies, and the cutoffs were lower than those of the fellow eyes (4half-1: OD 23.2, OS 4.80 cy/deg and 4half-2: OD 11.4, OS 23.1 cy/deg). The amblyopia cannot, however, be explained on the basis of refractive error as both monkeys had only a 1.00D difference between their eyes, and the refractive errors were normal (4half-1: OD +1.00D, OS Plano (PL) and 4half-2: OD PL, OS -1.00D).

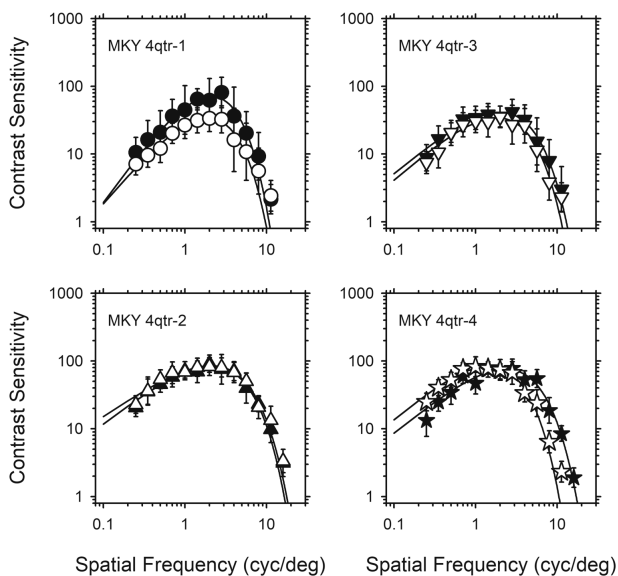
Contrast sensitivity functions for the four monkeys who had four quarter-hour periods of normal binocular vision are shown in [Figure 4](#). Only one monkey (4qtr-2) showed normal matched contrast sensitivity functions for the two eyes, with normal cutoff spatial frequencies (OD 16.5, OS 17.7 cy/deg). Monkey 4qtr-4 showed monocular functions that had normal shapes, but the position of the left eye curve was shifted to lower spatial frequencies than that of the right eye, resulting in a reduced high spatial frequency cutoff for the left eye (OD 17.2, OS 10.5 cy/deg). This monkey had myopic anisometropia, with the left eye being significantly more myopic than the right (OD -2.00D, OS -6.00D). Monkey 4qtr-1 showed a shift of the left eye curve to lower sensitivities over the peak but reduced high spatial frequency cutoffs for each eye (OD 10.8, OS 9.7 cy/deg). Finally, monkey 4qtr-3 showed a depression in sensitivity reflected by the reduced height of the curves for both

2 Non-continuous Hours BV/Day



**FIGURE 3.** Monocular spatial contrast sensitivity functions for monkeys who were prism reared with a total of 2 hours of normal binocular vision per day that were distributed into two 1-hour intervals (2hr-1 to 2hr-4) or four half-hour intervals (4half-1 and 4half-2). See Figure 1 for details.

One Non-continuous Hour BV/Day



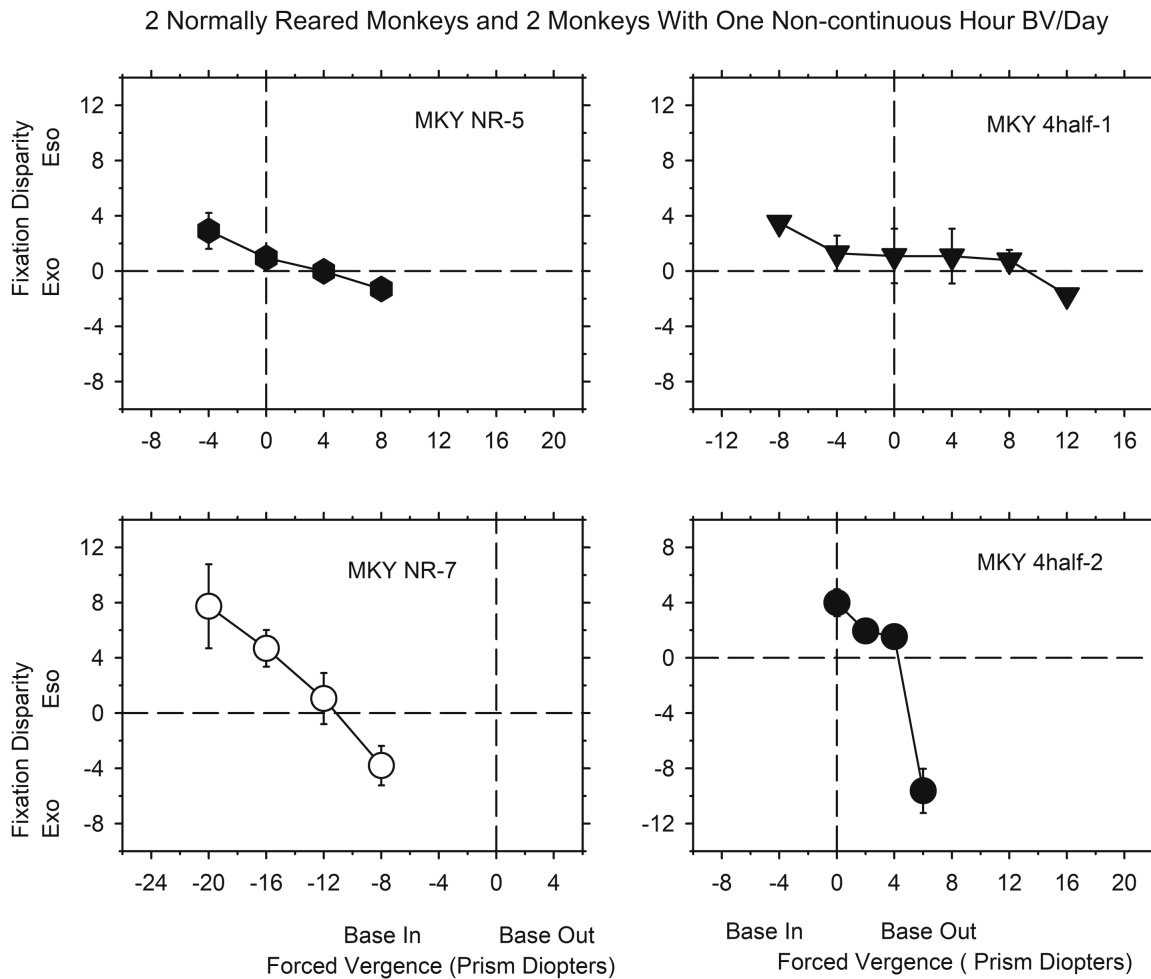
**FIGURE 4.** Monocular spatial contrast sensitivity functions for four monkeys who were prism reared with four quarter-hour periods of normal binocular vision per day. See Figure 1 for details.

Fixation Disparity and Interocular Alignment

Of all 14 prism-reared monkeys, monkey 4qtr-4 could not perform the dichoptic Vernier alignment task, even though he could distinguish laterality of the test target with each eye independently. Evidently, clinical suppression prevented monkey 4qtr-4 from seeing the right and left eye targets at the same time.

Figure 5 shows a normal forced-vergence fixation disparity curve from normally reared monkey NR-5 and, in contrast, curves from normally reared monkey NR-7 and both monkeys reared with four half-hour periods of normal binocular vision per day (4half-1 and 4half-2), all of whom had potential obstacles to stable motor fusion. The curve from normally reared monkey NR-5 is normal because base-in prism caused an overconverged (eso) fixation disparity, where his eyes were not exactly as diverged as the prism demand, and base-out prism caused an exo fixation disparity where he had a small diverged vergence error relative to the convergence demand of the prism. The function for monkey NR-5 is relatively flat with a slope of 0.35, indicating that there were only small vergence errors despite the vergence demands imposed by the prism. Where the curve crosses the x-axis indicates that his vergence error was reduced to zero with 4 BO prism. In contrast, normally reared monkey NR-7 showed a steeper curve with a slope of 0.96, indicating poorer vergence accuracy in response to prism but also a significant associated phoria of 11 BI. Monkey NR-7 viewed the stereoscopic stimuli with the 11 BI in addition to her refractive correction (OD +1.00D, OS +6.00D) and did have stereopsis. Monkey 4half-1 had a significant difference between the cutoff spatial frequencies for her two eyes (OD 23.2, OS 4.80 cy/deg) and so was monocularly amblyopic, yet she did have stereopsis. Her forced-vergence fixation disparity curve is also flat with a slope of 0.26, indicating

eyes and reduced high-frequency cutoffs (OD 13.0, OS 11.2 cy/deg). Refractive error cannot explain these variations from normal contrast sensitivity functions as the refractive errors were equal for the two eyes of each of these two monkeys and within a normal range (4qtr-1: +1.00 OU, 4qtr-3: PL OU).



**FIGURE 5.** Forced-vergence fixation disparity functions for normally reared monkeys NR-5 and NR-7 and for two monkeys who were prism reared and allowed four half-hour periods of normal binocular vision per day. The x-axis intercept indicates the prism required to neutralize the fixation disparity (i.e., for monkey NR-7 = 11 prism diopters base-in).

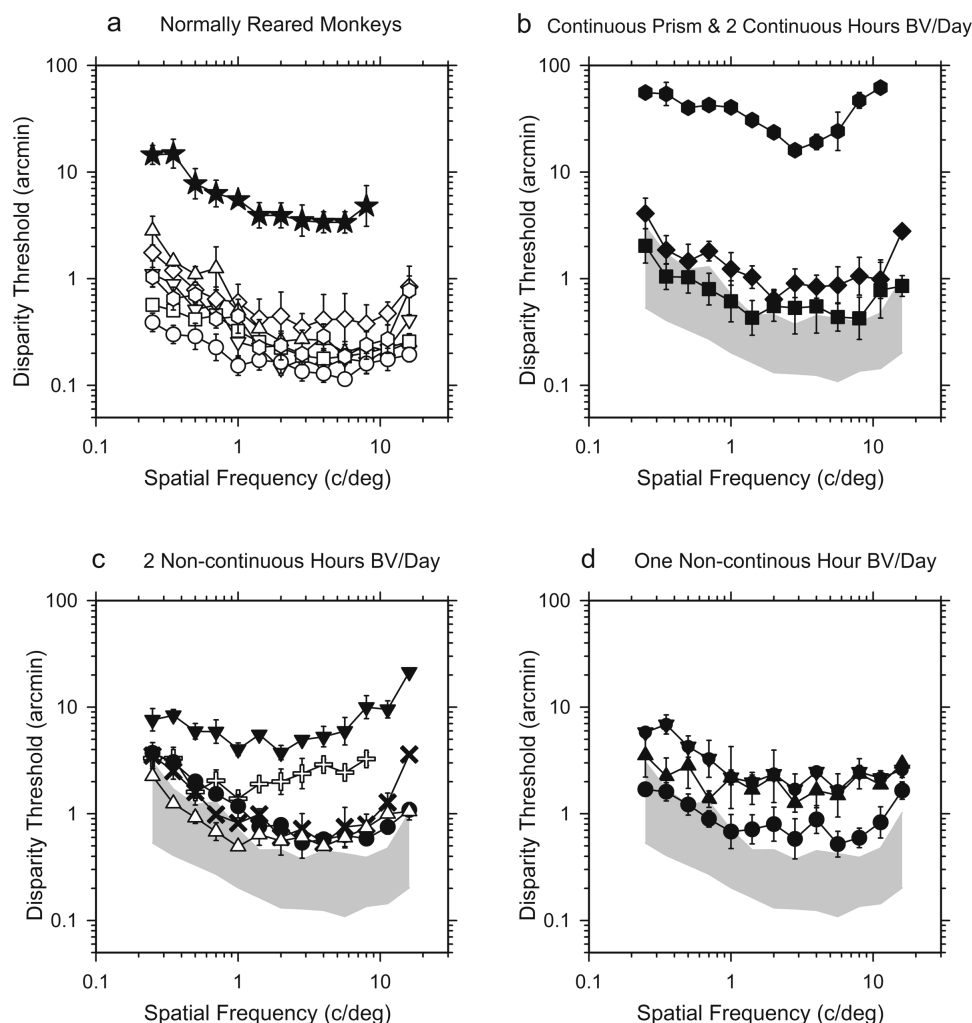
relatively good vergence compensation for prism. She also viewed the stereoscopic stimuli with her associated phoria of 10 BO in addition to her refractive correction and had stereopsis. Monkey 4half-2 did not have stereopsis, despite being less amblyopic than monkey 4half-1 (4half-2: OD 11.4, OS 23.1 cy/deg). Her forced-vergence fixation disparity curve is very steep with a slope of 2.3, indicating large errors in vergence with prism stress, revealing that unstable fusion likely prevented her from being able to perform the stereo discriminations.

**Local Stereopsis**

Three prism-reared monkeys were unable to discriminate stereoscopic depth on the basis of binocular disparity (CP-2, 4half-2, and 4qtr-4). As discussed in the previous section, monkey 4qtr-4 had suppression and monkey 4half-2 had unstable motor fusion, which prevented these two monkeys from demonstrating stereopsis. Monkey CP-2 was severely bilaterally amblyopic (OD 3.9, OS 5.7 cy/deg) likely owing to his bilaterally high refractive error (OD +11.00, OS +11.00). All three monkeys were extensively trained but could not distinguish stereoscopic depth without the contrast cue used during training.

Depth discrimination thresholds are plotted against the grating spatial frequency of the Gabor stimuli for the normally reared monkeys in Figure 6a. Monkeys whose data are represented by the open symbols showed a decrease in disparity threshold over low to mid spatial frequencies to an average minimum of  $0.20 \pm 0.08$  arcmin (12 arcsec) at about 4.2 cy/deg, with the thresholds remaining relatively constant, only slightly increasing toward the highest spatial frequencies. In subsequent panels of Figure 6, the average of data from these normal monkeys  $\pm 2$  SD are shown as a gray area that very closely approximates the range of the individual functions from these normal monkeys shown in this panel. Monkey NR-7 (filled stars) was reared normally but had hyperopic anisometropia, bilateral amblyopia, and a significant associated phoria. Her disparity threshold function is the same shape as those of normal monkeys but is shifted to higher disparities so that her best stereopsis was 3.4 arcmin (204 arcsec) at 5.64 cy/deg.

In Figure 6b, data from monkeys reared 4 weeks with continuous prism (CP-1: hexagons) and 2 continuous hours of normal binocular vision per day (C2hr-1: squares and C2hr-2: diamonds) are superimposed on the data from normally reared monkeys. Monkey CP-1 showed a 10-fold increase in disparity threshold across all spatial frequencies,



**FIGURE 6.** Depth discrimination thresholds are plotted as a function of the spatial frequency of the Gabor carrier grating. *Data points:* average of three threshold determinations; *error bars:* standard deviations. (a) Normally reared monkeys including monkey NR-7 (*filled stars*). (b) *Hexagons* are data from one monkey reared with continuous prism (CP-1); *squares* (C2hr-1) and *diamonds* (C2hr-2) are data from the two monkeys who were allowed 2 continuous hours of normal binocular vision per day, superimposed on the average  $\pm 2$  SD of normal monkeys (*gray area*). (c) Data from one monkey prism reared with four half-hour periods of normal binocular vision per day (4half-1: *down-triangles*) and four monkeys reared with two 1-hour periods of normal binocular vision per day (2hr-1: *up-triangles*; 2hr-2: *X*; 2hr-3: *circles*; 2hr-4: *plus signs*) superimposed on the average  $\pm 2$  SD of normal monkeys (*gray area*). (d) Data from three prism-reared monkeys with four quarter-hour periods of normal binocular vision per day (4qtr-1: *circles*; 4qtr-2: *up-triangles*; 4qtr-3: *down-triangles*) superimposed on the average  $\pm 2$  SD of normal monkeys (*gray area*).

and his best stereopsis was 16.0 arcmin (960 arcsec) with the 2.82 cy/deg Gabor. Monkey C2hr-1, who also wore prism for 4 weeks but had 2 continuous hours of normal vision per day, showed near-normal stereopsis of 0.43 arcmin (25.8 arcsec) with the 1.41 cy/deg Gabor. Monkey C2hr-2, who also had 2 continuous hours of normal binocular vision per day but was prism reared for 6 weeks, showed only a one-octave elevation in threshold, and her best stereopsis was 0.64 arcmin (38.4 arcsec) with the 2-cy/deg target. In this set of four monkeys (including stereoblind CP-2), the two monkeys that were prism reared for the longer duration of 6 weeks (CP-2 and C2hr-2) had more severe deficits than the two monkeys that were prism reared for the shorter duration of 4 weeks (CP-1 and C2hr-1). All data are listed in the [Table](#).

In [Figure 6c](#), data from all monkeys allowed 2 noncontinuous hours of binocular vision per day are plotted: these

are four monkeys with two 1-hour periods (2hr-1 to 2hr-4) and one monkey with four half-hour periods (4half-1: down-triangles) of normal binocular vision per day. Monkey 2hr-1 (up-triangles) showed the best stereopsis of this group, with thresholds similar to those of normal monkeys (*gray area*). His best stereopsis was 0.49 arcmin (29.4 arcsec) at 1 cy/deg. Monkeys 2hr-2 (X) and 2hr-3 (circles) had near-normal thresholds across all spatial frequencies, and both had best stereopsis of 0.54 arcmin (32.4 arcsec): monkey 2hr-2 at 4.0 cy/deg and monkey 2hr-3 at 2.82 cy/deg. Monkey 2hr-4 (plus signs) showed the same disparity thresholds over low spatial frequencies as did monkeys 2hr-2 and 2hr-3, but starting at 2.0 cy/deg, her disparity thresholds elevated dramatically over the range of higher spatial frequencies. It is likely that she could see the targets, as her spatial frequency cutoffs (OD 17.9, OS 17.3 cy/deg) were very similar to those of monkey 2hr-2 (OD 17.0, OS 19.3 cy/deg).



Monkey 4half-1 (down-triangles) had the poorest stereopsis of the group with 3.75 arcmin (228 arcsec) with 2.0-cy/deg Gabor targets. The duration of prism rearing had little effect on the stereopsis of the four monkeys reared with two 1-hour periods of binocular vision per day as all four monkeys had very similar thresholds. If anything, the effect of duration was opposite what was expected as the monkey with the best stereopsis (2hr-1) was prism reared for 6 weeks, and the monkey with the poorest stereopsis of this group (2hr-4) was prism reared for the shorter 4-week duration. Monkeys reared with four half-hour periods of binocular vision per day did show the expected effect of rearing duration in that only the monkey that was prism reared for the shorter 4-week duration showed stereopsis (4half-1), while the monkey prism reared for the longer 6-week duration (4half-2) did not.

In light of results from animals reared with a total of 2 hours distributed into four half-hour periods of normal vision per day, it was surprising that monkeys reared with four quarter-hour periods of normal vision had better stereopsis. The results are shown in Figure 6d. One monkey, 4qtr-1 (circles), had near-normal stereopsis of 0.52 arcmin (31.2 arcsec) with 5.64-cy/deg targets. The two other monkeys (4qtr-2: up-triangles and 4qtr-3: down-triangles) had disparity thresholds about a 1 log unit larger than normal (4qtr-2: 1.26 arcmin with 2.82-cy/deg Gabors and 4qtr-3: 1.65 arcmin with 5.64-cy/deg targets). All of the monkeys that had 1 hour of normal vision per day were prism reared for 6 weeks.

Comparing the data across the groups of prism-reared monkeys (Figs. 6b, 6c, 6d), the pattern of results is strikingly similar. It is clear that the one animal from each group that had the best stereopsis performed within the range of normal animals. These three monkeys were as follows: for Figure 6b, monkey C2hr-1 (squares); for Figure 6c, monkey 2hr-1 (up-triangles); and for Figure 6d, monkey 4qtr-1 (circles). Monkeys 2hr-1 and 4qtr-1 were prism reared for 6 weeks, while monkey C2hr-1 was prism reared for 4 weeks, so duration of prism rearing was not the common denominator. In fact, there are no obvious similarities between these best performers. Across groups, the worst performers were as follows: for Figure 6b, monkey C2hr-2 (diamonds) (not CP-1 [hexagons] because he was a control animal reared with continuous prism); for Figure 6c, monkey 4half-1 (down-triangles); and for Figure 6d, monkey 4qtr-3 (also down-triangles). Again, duration of prism wear among this group of poor performers was varied: monkey 4half-1 was prism reared for 4 weeks, and monkeys C2hr-2 and 4qtr-3 were prism reared for 6 weeks. Monkeys whose performance was between the extremes were as follows: for Figure 6c, monkeys 2hr-2 (X), 2hr-3 (circles), and 2hr-4 (plus signs), and for Figure 6d, monkey 4qtr-2 (up-triangles). Duration of prism wear was again different, with monkeys 2hr-2 and 4qtr-2 with 6 weeks and monkeys 2hr-3 and 2hr-4 with 4 weeks of prism wear. There is a curious similarity in the shape of the curves for monkeys 2hr-4 and 4qtr-2 in that they mirror thresholds by the best performers over low spatial frequencies to about 1.0 cy/deg, and then their thresholds rise to close to those of the worst performers over higher spatial frequencies. Both monkeys had good equal spatial frequency cutoffs (2hr-4: OD 17.9, OS 17.3 cy/deg and 4qtr-2: OD 16.5, OS 17.7 cy/deg), so it is not that these monkeys could not see the targets. Best-performing monkey 2hr-1 had similar spatial frequency cutoffs (OD 17.8, OS 19.8 cy/deg), and 4qtr-1 had worse (OD 10.8, OS 9.70 cy/deg).

## Global Stereopsis

Depth discrimination thresholds as a function of the correlation in polarity between random dots seen by the right and left eyes are shown in Figure 7. Monkeys NR-2 and NR-4 were not tested with random dot targets, and monkey NR-1 was not basing his responses on binocular stereoscopic depth as they were similar with one eye occluded. Data for the remaining normally reared monkeys are shown in Figure 7a. The average of best thresholds for monkeys NR-3 (circles), NR-5 (hexagons), and NR-6 (down triangles) was  $0.16 \pm 0.037$  arcmin ( $9.60 \pm 2.22$  arcsec) and was achieved with 100% correlation. Over decreasing correlations, their disparity thresholds decreased with slopes of about  $-0.50$  (NR-5 and NR-6) and  $-1.0$  (NR-3). Monkey NR-7 (stars) had the highest thresholds of all the monkeys, with a best threshold of 3.4 arcmin (204 arcsec) and could not perform the task with correlations below 50%.

Figure 7b shows depth discrimination thresholds for monkeys CP-1 (hexagons), reared with continuous prism-wear, and for prism-reared monkeys C2hr-1 (squares) and C2hr-2 (diamonds), who each had 2 continuous hours of normal vision each day. Data from these monkeys are superimposed on the fitted data from normal monkeys. Monkey CP-1 had his best stereopsis of 3.30 arcmin (200 arcsec) with 100% correlation. As with the local stereo targets, monkey C2hr-1 had near-normal best stereopsis (0.44 arcmin or 26.4 arcsec) with 80% correlation. Monkey C2hr-1 was prism reared for 4 weeks, while monkey C2hr-2 was prism reared for 6 weeks and, due to the longer duration of abnormal visual experience, also had poorer global stereopsis. Her best threshold was 0.85 arcmin (51.0 arcsec).

In Figure 7c, data from monkeys reared with 2 nonconsecutive hours of normal vision per day are superimposed on the fitted data from normal monkeys. Monkey 4half-1 (down-triangles) had the poorest stereopsis of the group with a best threshold of 4.2 arcmin (252 arcsec) and was given four half-hour periods of normal vision per day. All the other monkeys whose data are shown in this panel had two 1-hour periods of normal vision per day (2hr-1 to 2hr-4). Their functions are closer to those of normal monkeys, approximately evenly spaced and in the same order of performance as with local stereotargets (Figure 6c). Of this group, monkey 2hr-1 (up-triangles) had thresholds near normal (best was 0.21 arcmin or 12.6 arcsec), and monkey 2hr-4 (plus signs) performed worst with best stereopsis of 0.66 arcmin or 39.6 arcsec.

In Figure 7d, data from monkeys allowed 1 hour (four quarter-hour periods) of normal vision daily are plotted in comparison to the fitted data from normal monkeys. As with the previous groups, data from the three monkeys with global stereopsis range from near normal (4qtr-1: circles) to close to the poorest stereopsis (4qtr-3: down-triangles), with one monkey in between (4qtr-2: up-triangles). Monkey 4qtr-1's best stereopsis was 0.26 arcmin (15.6 arcsec) with 80% correlation, better than double the average of that of normal monkeys (9.6 arcsec). Monkey 4qtr-3's stereopsis is among the poorest, with her best stereopsis of 2.84 arcmin (170 arcsec), and monkey 4qtr-2 falls between these two extremes with his best stereopsis of 0.66 arcmin (39.6 arcsec). Both of these best thresholds were with 90% correlation targets.

The order of best to worst performers with random dot targets depicted in each panel of Figure 7 is very similar to that observed with local stereo-targets in the corresponding panels of Figure 6. In that these monkeys were able to distinguish stereoscopic depth with random dot targets, it

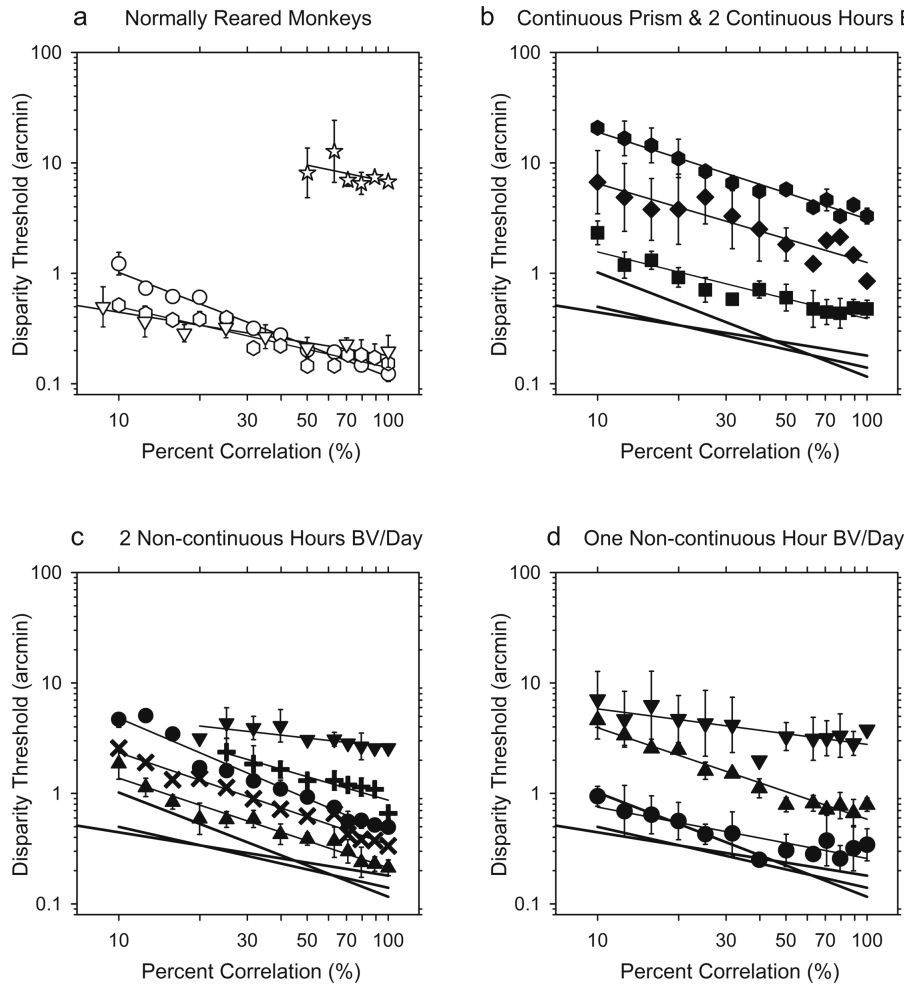


FIGURE 7. Depth discrimination thresholds are plotted as a function of the correlation of dot polarity between left and right eye random dot stimuli. *Data points:* average of three threshold determinations; *error bars:* standard deviations. Panels are same as Figure 6, except that the data from normal monkeys are represented as the lines fitted to individual monkey's data.

is likely that they maintained bifoveal fixation and did not become overtly strabismic as a consequence of the prism rearing.

In order to summarize the data from treated animals, their best local and global thresholds were normalized to the average of normal monkeys (0.2 arcmin for local and 0.16 arcmin for global stereopsis) and plotted in Figure 8. The most striking feature of this comparison is just how good the outcome was for most monkeys despite their prolonged daily experience of optical strabismus. Six monkeys show thresholds that are better than 40 arcsec, which is only threefold larger than the average of normal monkeys. This level of stereopsis is still considered fine foveal stereopsis and in human observers is considered clinically normal. At the same time, it is more clearly evident that good stereopsis is more likely with longer continuous durations of normal binocular vision as the results are more variable with multiple shorter durations.

### DISCUSSION

The main result of this study is that stereopsis can be preserved in monkeys by providing multiple short periods of normal binocular vision every day during otherwise

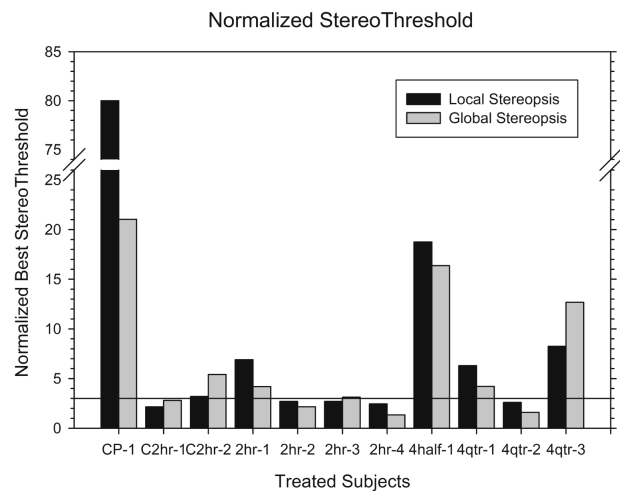


FIGURE 8. For all treated monkeys who had stereopsis, the best threshold is divided by the average of best thresholds from normal monkeys (0.2 arcmin for local and 0.16 arcmin for global thresholds). *Black bars* are for local stereopsis and *gray bars* are for global stereopsis. *Reference line:* three times the threshold for normal monkeys. Note the break in the vertical axis.

constant optical strabismus. Previous work indicated that a single continuous 2-hour daily period of normal binocular vision largely preserved stereopsis.<sup>4</sup> This investigation has extended that finding to show that the 2-hour daily period of normal binocular vision does not have to be continuous to preserve stereopsis. The “spacing effect,” in which performance is better following multiple short practice sessions compared to a single long session, was not unequivocally supported. However, shorter multiple daily periods that totaled only 1 hour of daily normal binocular vision did rescue stereopsis in three of four animals, confirming that the effects of normal binocular visual experience vastly outweigh the effects of abnormal binocular visual experience on vision development.

### Methodologic Considerations

Prism rearing is an excellent experimental manipulation for these investigations because it allows precise control of the timing and nature of the visual experience. While the monkey is looking through the prism, the visual experience is virtually identical to that of naturally occurring strabismus in that there is “diplopia” or double vision, but also “confusion,” in which two things appear to be in the same location in space. Prism wear simulates comitant strabismus where the angle of the deviation is the same in all directions of gaze, again similar to comitancy in infantile esotropia. The other major advantage to prism rearing over pharmacologic or surgical strabismus is that when the prisms are removed, binocular eye alignment and superimposition of images from the two eyes are immediately restored to normal and remain so for the period during which the prisms are off.

Prism rearing was purposefully delayed until animals were 4 weeks of age, as by this time, eye alignment and motor control of eye movements have largely been established, ensuring that animals rarely become strabismic as a consequence of prism rearing.<sup>35</sup> The maturity of the motor system ensures that the sensory experiences of strabismus while viewing through the prism and normal binocular fusion while not viewing through the prism are actually occurring. No animal in this study developed overt strabismus, as indicated by their forced-vergence fixation disparity functions, confirming that the visual experiences both with and without the prisms were as intended.

The timing of the start of optical strabismus in this experiment closely approximates the time at which infantile esotropia begins in human infants, and this similarity in timing strengthens the applicability of these results to the human condition. Infantile esotropia is not present at birth but develops over the first 6 months of life.<sup>11,12</sup> Considering that monkeys mature faster than humans by a factor of four,<sup>47</sup> the introduction of optical strabismus at 4 weeks of age in our monkeys is equivalent to infantile esotropia becoming established by 4 months of age in a human infant. By this time, both monkeys<sup>6</sup> and humans<sup>7,8</sup> have similarly developed the neural foundations for stereopsis.

### Developmental Time Course

During the first 4 weeks of life, the sensory system has begun to develop, including mechanisms that are sensitive to binocular spatial disparity. In monkeys, behavioral stereopsis emerges at 3 to 4 weeks of age on average, but the emergence of stereopsis varies significantly between indi-

viduals from 1 to 8 weeks of age.<sup>47</sup> Similarly, there is significant variability between individual human infants regarding the age at which stereopsis emerges.<sup>48</sup> In our monkeys, the introduction of prisms at 4 weeks of age would have interrupted the emergence of stereopsis to varying degrees, depending on each individual's unique developmental time course. If stereopsis had not yet emerged by the time prisms were introduced, that animal might be less likely to have stereopsis following prism wear.

The timing of prism rearing was meant to coincide with the critical period of development of stereopsis. For both infant humans and normally reared monkeys, disparity sensitivity is fine-tuned during the critical period so that following its emergence, stereopsis develops rapidly to near-adult levels of 1 arcmin within 5 to 6 weeks.<sup>47,48</sup> In contrast, constant strabismus during the critical period causes an “extinction” or elimination of disparity-sensitive mechanisms so that disparity sensitivity disappears completely.<sup>8</sup> This was the expected outcome for our control monkeys who wore prism constantly, and this was the outcome for monkey CP-2, who experienced constant optical strabismus for 6 weeks.

The daily periods of normal binocular visual experience were hypothesized to prevent elimination and preserve the emergent disparity-sensitive mechanisms. During the 4 to 6 weeks when experimental animals were wearing prism, normal animals were rapidly improving in disparity sensitivity. It is unknown whether the experimental animals only maintained the level of disparity to which they had become sensitive to prior to prism wear (arrest of development), regressed, or improved during the prism rearing. It may be that the process depended on the extent to which stereopsis had emerged by the time prisms were introduced and the length and number of periods of normal binocular vision allowed each day during prism wear. Certainly, there was the most consistency in result with the two monkeys that were allowed 2 continuous hours of normal binocular vision per day (C2hr-2 and C2hr-2) in that the monkey that was prism reared for the longer duration of 6 weeks (C2hr-2) had slightly reduced stereopsis relative to the monkey that was prism reared for the shorter duration of 4 weeks (C2hr-1). For these monkeys, it could be that 2 continuous hours of normal binocular vision allowed for disparity-sensitive mechanisms to improve somewhat during the critical period during which prisms were being worn, as both had disparity thresholds that were at the upper limit of the range of normal.

The stereoscopic results are not as clear for monkeys who experienced shorter more numerous periods of normal binocular vision. Within the group that experienced 2 noncontinuous hours of normal binocular vision and within the group that experienced 1 noncontinuous hour of normal binocular vision, there was one animal in each group with good stereopsis (2hr-1 and 4qtr-1). Both of these animals were prism reared for the longer duration of 6 weeks. The difference between these monkeys and their peers could be that stereopsis may have emerged prior to the introduction of prism, so that the normal binocular visual experience that was provided was sufficient to maintain and/or improve stereopsis during prism wear. On the other hand, within each group were animals with poor stereopsis (4half-1 and 4qtr-3). For these monkeys, stereopsis may have not yet emerged by the time prisms were introduced, so that the amount of normal binocular visual experience provided could not outweigh the destructive effects of the imposed

strabismus. Both of these monkeys had normal refractive errors, but monkey 4qtr-3 had low but equal grating acuities (OD 13.0, OS 11.2 cy/deg) and monkey 4half-1 had unilateral amblyopia (OD 23.2, OS 4.80 cy/deg), which could have also resulted from the imposed strabismus.<sup>46</sup>

By 10 weeks of age, the critical period for the development of stereopsis had ended, so stereopsis in normal monkeys had matured to adult levels while our experimental animals had just finished their prism rearing. All animals were allowed unrestricted normal binocular vision following the end of prism rearing, but whether or not disparity sensitivity continued to mature in the prism-reared animals is debatable. Certainly, the critical period during which normal development can be interrupted by abnormal visual experience is shorter than the time during which functional recovery from setbacks can still occur.<sup>10,37,49-51</sup> Because all monkeys had the same postrearing experience, whether or not stereopsis improved during this time may have depended on the degree to which stereopsis had developed up to this point, with monkeys that had less damage done able to continue to improve.

### Control Animals

There were two sets of control animals for this study: normally reared monkeys and monkeys reared with continuous prism. Six normally reared monkeys (NR-1 to NR-6) provided uniformly normal data. One normally reared monkey (NR-7) had naturally occurring anisometropia (OD +1.00D, OS +6.00D), and although the expectation based on this anisometropia was that she would have unilateral amblyopia, she was bilaterally amblyopic (OD 10.8, OS 10.7 cy/deg). Her associated phoria was also significant (11 BI). Despite these impediments, she did have stereopsis, although it was poorer than any of the experimental animals with stereopsis. The reason her data were included is to emphasize the devastating effect that optical strabismus had in extinguishing stereopsis in the two monkeys who did not have stereopsis and also to highlight just how good the stereopsis rescued by periods of normal binocular vision was.

### Monkeys Without Stereopsis

If the daily periods of normal binocular visual experience did nothing to preserve stereopsis, we would expect that all of our animals would express the sensory sequela of constant strabismus, including suppression or anomalous correspondence, possibly amblyopia, and reduced or absent stereopsis. Two control animals in this investigation were reared with constant strabismus, and the one animal that was prism reared for the longer duration (CP-2 for 6 weeks) had no demonstrable stereopsis and bilateral amblyopia. As a control experiment, one monkey who did have stereopsis (C2hr-1) was blurred with lenses so that she had reduced contrast sensitivity comparable to the contrast sensitivity of monkey CP-2 and then was tested for local stereopsis with these blurring lenses in place. Even with the imposed reduction in contrast sensitivity, monkey C2hr-1 still had stereopsis, although her thresholds were shifted to larger disparities, especially over higher spatial frequencies.<sup>4</sup> These results indicate that the control monkey CP-2 did not lack stereopsis because he could not see the targets, he lacked stereopsis because he did not have functional disparity-sensitive mechanisms, and that these had been destroyed by the constancy of the strabismus. This was the outcome

that was expected with the control animals and all animals if the periods of normal binocular visual experience had no effect.

Two monkeys (4half-2 and 4qtr-4) reared with multiple shorter periods of normal binocular vision did not have stereopsis but instead showed the damaging effects of the imposed strabismus. Monkey 4half-2 had four 30-minute periods of normal binocular experience during the longer 6-week duration of otherwise constant strabismus. Monkey 4half-2 had moderate unilateral amblyopia, although because monkey 4half-1 was also amblyopic but did have stereopsis, the amblyopia was not considered the cause of monkey 4half-2's lack of stereopsis. Monkey 4half-2, however, did have a very steep forced-vergence fixation disparity function indicating that motor fusion was tenuous and that it was likely that sensory fusion was tenuous as well. Unstable binocular fusion is understandably a common and not unexpected result of the strabismus. Monkey 4qtr-4 was allowed four 15-minute periods of normal binocular vision per day while prism reared for 6 weeks. Because monkey 4qtr-4 could not see targets dichoptically, it was inferred that he had developed suppression as a result of the strabismic visual experience. Suppression is an adaptation to strabismus that commonly develops during the critical period in human strabismics and not at all unexpected considering the extent and timing of the imposed strabismic experience. So, for these three monkeys, their inability to demonstrate stereopsis was not a failure of the experiment; it was the expected outcome of the constancy of the strabismus, which was timed to coincide with the critical period for the development of stereopsis, where it would be the most damaging to normal binocular visual development.

### Monkeys With Stereopsis

In contrast to monkeys who did not have stereopsis, six monkeys had local stereopsis better than 40 arcsec (C2hr-1, C2hr-2, 2hr-1, 2hr-2, 2hr-3, and 4qtr-1). Two of these monkeys did have 2 continuous hours of normal binocular vision per day (C2hr-2 and C2hr-2), but monkeys 2hr-1, 2hr-2, and 2hr-3 had two 1-hour periods and monkey 4qtr-1 had four 15-minute periods of normal binocular vision per day. For these monkeys, the provision of even these short periods of normal binocular vision compared to the much longer 10-hour or 11-hour periods of optical strabismus per day successfully preserved high-grade stereopsis. This result was remarkable, considering that very few postsurgical human infantile esotropes achieve this degree of stereosensitivity.<sup>14,18-25</sup>

Three other monkeys who retained stereopsis (2hr-4, 4qtr-2, and 4qtr-3) had disparity thresholds that were about 100 arcsec, while the prism-reared monkey with the poorest stereopsis (4half-1) had a disparity threshold of 225 arcsec. These results are still very good, especially when compared to the outcome of monkeys for whom stereopsis was not preserved and the outcome of most postsurgical human infantile esotropes.<sup>14,18-25</sup> Even this subnormal level of stereopsis requires peripheral sensory and motor fusion, and in postsurgical cases, sensory fusion promotes motor fusion, resulting in better prognoses for maintenance of eye alignment and a reduction in subsequent alignment surgeries.<sup>21,52-54</sup> In this regard, even when some stereopsis is preserved, there is a benefit.

## Comparison to Studies in Kittens

The results of this study are not directly comparable to those reported by Mitchell et al.<sup>5</sup> in kittens, possibly because of differences in the visual manipulations imposed in addition to the 2 continuous hours of normal binocular vision. In the Mitchell et al.<sup>5</sup> study, two of three kittens did not demonstrate stereopsis following a rearing protocol of 2 hours of binocular vision followed by 5 hours of monocular occlusion, then 17 hours of darkness each day from 4 to 8 weeks of age. In their previous studies, control kittens experienced continuous monocular occlusion,<sup>55,56</sup> but no control experiments had been performed on kittens to determine the impact that the longer 17-hour daily duration of darkness had on stereopsis.

## Recommendations

Specific interventions that provide binocular visual experience to strabismic infants are beyond the scope of this investigation but may include optical aids in combination with repeating “wallpaper” targets to help superimpose images from the two eyes. For parents of strabismic infants who question whether interventions intended to provide binocular vision would be of any value, especially when such measures might be difficult over extended periods of time, the answer is yes. Our results suggest that although longer continuous durations of normal binocular visual experience are more consistently likely to result in better binocular function, there is not a minimum requirement of 2 continuous hours per day. Instead, it appears that even a shorter total time per day divided into shorter periods can preserve stereopsis. Our recommendation would be that because of the evidently strong effect normal visual experience has on developing binocular mechanisms, that any and every opportunity to provide binocular experience should be exploited, because there may be some positive effect. We would advise parents to not be discouraged when they are unable to sustain binocular vision in their strabismic infant but to provide what binocular visual experience they can, to preserve binocular function until the eyes can be surgically aligned.

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