Potency of Myopic Defocus in Spectacle Lens Compensation

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Purpose. Previous studies have shown that chick eyes compensate for positive or negative lenses worn for brief periods if the chicks are in darkness the remainder of the time. This study was undertaken to determine whether chicks can compensate for brief periods of lens wear if given unrestricted vision the remainder of the time. Previous studies have also shown that chick eyes alternately wearing positive and negative lenses for brief periods compensate for the positive lenses. The current study sought to determine whether brief periods of positive lens wear can outweigh daylong wearing of negative lenses.

Methods. Chicks wore +6 D or +10 D lenses for between 8 and 60 min/d, in two to six periods and wore either no lenses or negative lenses for the remainder of the 12-hour daylight period. Refraction and ultrasound biometry were performed before and after the 3-day-long experiments.

Results. Wearing positive lenses for as little as 12 min/d (six periods of 2 minutes) with unrestricted vision the remainder of the time caused eyes to become hyperopic and reduced the rate of ocular elongation. These effects also occurred when the scene viewed was beyond the far point of the lens-wearing eye and thus was myopically blurred. Even when chicks wore negative lenses for the entire day except for 8 minutes of wearing positive lenses, the eyes compensated for the positive lenses, as though the negative lenses had not been worn. When chicks wore binocular negative lenses for the entire day except for 8 minutes of wearing a positive lens on one eye and a plano lens on the other, the eye wearing the positive lens became less myopic than the eye wearing the plano lens.

Conclusions. Brief periods of myopic defocus imposed by positive lenses prevent myopia caused by daylong wearing of negative lenses. This implies that periods of myopic and hyperopic defocus do not add linearly. If children are like chicks and if the hyperopic defocus of long daily periods of reading predisposes a child to myopia, regular, brief interruptions of reading might have use as a prophylaxis against progression of myopia. (*Invest Ophthalmol Vis Sci.* 2003;44:2818–2827) DOI:10.1167/iovs.02-0606

Eyes attain and maintain emmetropia (eye length matched to focal length) by using visual feedback to adjust the position of the retina in relation to the optics of the eye. This effect has been shown by experiments in which animals compensated for the defocus imposed by spectacle lenses by adjusting eye growth with the result that functional emmetropia (while the lenses are worn) was swiftly regained.[1–3] When eyes are fitted with positive lenses (creating myopic blur; distant objects imaged in front of the retina), ocular elongation slows, and choroidal thickness increases, thereby moving the retina closer to the focal plane. In contrast, when eyes are fitted with negative lenses (hyperopic blur; images behind the retina), ocular elongation accelerates, and choroidal thickness decreases, thereby pulling the retina back toward the focal plane. The phenomenon of spectacle lens compensation has been shown in chicks,[1,2] rhesus monkeys,[4] marmosets,[5] tree shrews (Siegwart JT, Norton TT, ARVO Abstract 2482, 1993), and guinea pigs (McFadden S, Wallman J, ARVO Abstract 3504, 1995).

Given that the eye can adjust itself to imposed defocus in this way, it is possible that children become myopic by compensating for the slight hyperopia experienced during reading. Thus "school myopia" may result from the normal operation of the emmetropization mechanism revealed by these animal experiments, rather than because of any physiological defect or disease process. Because vision in daily life involves periods of both myopic and hyperopic defocus, understanding how myopia develops may require understanding the dynamics of lens compensation.

In a previous study,[6] we have shown two characteristics of lens compensation in chicks that may be relevant to understanding human myopia. First, we found that brief periods of lens wear, repeated frequently each day, can produce robust compensation if the birds are in darkness the remainder of the time. This shows an enduring effect of the defocus briefly imposed by wearing the lenses. Second, we found that if positive and negative lenses are worn alternately, the eye responds to the positive lens much more strongly than to the negative lens, even if the visual stimuli are beyond the far point of the eye while wearing the positive lenses and therefore are myopically blurred (images in front of retina). This greater responsiveness to positive lenses is consistent with findings that compensation for positive lenses occurs with fewer hours of daily lens wear than does compensation for negative lenses, if the chicks have normal vision the remainder of the time.[7]

If similar processes take place in children, myopic progression may be reduced by interrupting reading with appropriately timed periods of viewing in-focus or myopically defocused objects. To explore this possibility in an animal model, we assessed the potency of interrupting continuous negative lens wear (which presumably imposes hyperopic defocus) with brief periods of wearing either positive lenses or plano (zero-powered) lenses. We found that both lenses, but especially the positive lenses, worn briefly several times a day, can cancel the effect of much longer periods of negative lens wear.

Materials and Methods

Animals

White Leghorn chicks (*Gallus gallus domesticus*, of the Hyline W-98 strain) were obtained from Truslow Farms, Chestertown, MD. (One experiment, experiment 3, was performed both with this strain and with Cornell K-strain White Leghorns, obtained from Cornell University, Ithaca, NY; because we did not find any statistically significant

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Supported by National Eye Institute Grant EY-02727 and Division of Research Resources Grant RR-03060, National Institutes of Health, Bethesda, Maryland.

Submitted for publication June 19, 2002; revised October 18, 2002, and January 15, 2003; accepted February 24, 2003.

Disclosure: **X. Zhu**, None; **J.A. Winawer**, None; **J. Wallman**, None

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Table 1. Summary of Treatment Protocol for the Three Experiments

Experiment	Group	Lens for Episodes	Lens for Rest of Day	Daily Episodes	Total per Day (min)	Schedule of Episodes	*n*
1: Brief episodes of positive or negative lens. Unrestricted vision the rest of the day. Fellow eye untreated.	1	+6 D	None	30 min, 2×	60	8 AM, 8 PM	20*, 16
	2	+6 D	None	15 min, 4×	60	9 AM, 12:30, 4, 7:30 PM	10†
	3	+6 D	None	10 min, 6×	60	9, 11 AM, 1, 3, 5, 7 PM	16
	4	+6 D	None	2 min, 6×	12	9, 11 AM, 1, 3, 5, 7 PM	21
	5	+10 D‡	None	2 min, 6×	12	9, 11 AM, 1, 3, 5, 7 PM	10
	6	−15 D	None	2 min, 6×	12	9, 11 AM, 1, 3, 5, 7 PM	14
2: Brief episodes of positive lens. Negative lens the rest of the day. Fellow eye untreated.	7	+6 D	−6 D, monocular	15 min, 4×	60	9 AM, 12:30, 4, 7:30 PM	8
	8	+6 D	−6 D, monocular	2 min, 4×	8	9 AM, 12:30, 4, 7:30 PM	8
	9	−6 D	−6 D	Continuous			9
	10	+6 D	+6 D	Continuous			12
3: Brief episodes of positive lens (one eye) or plano lens (fellow eye). Binocular negative lenses the rest of the day.	11	+6 D (one eye), plano (fellow eye)	−6 D, binocular	2 min, 4×	8	9 AM, 12:30, 4, 7:30 PM	13§

Experiment for group 1 was performed on two separate occasions, with data reported separately for each.
* Refractions measured for only nine birds.
† Refractions measured for only five birds.
‡ Scene viewed was beyond far point.
§ Six birds of the Hyline W-98 strain and seven birds of the Cornell K strain were used.

differences between the strains in the degree of compensation in this particular paradigm, results were pooled for analysis.) Before the experiments started, chicks were reared in heated brooders under fluorescent lighting (lights on at 8 AM, off at 10 PM). During the experiments chicks were housed in a heated, sound-attenuated 76 × 61-cm chamber, with the lights on from 9 AM to 9 PM, except as noted for experiment 1. Food and water were provided ad libitum. Care and use of animals adhered to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. Experiments started when the chicks were 1 week old and lasted for 3 days.

Lenses

We used either PMMA plastic lenses, with a back optic radius of 7 mm, or glass lenses (which were not conspicuously curved) of the following powers: 0 (plano), +6, +10, −6, and −15 D. The positive lenses were glass, the plano lenses were plastic, and the negative lenses were either plastic or glass. The lenses, which were 12 mm in diameter, were glued between rigid plastic rings and Velcro rings, which were attached to mated Velcro rings glued to the feathers around the chicks' eyes. Lenses were cleaned at least twice daily. For experiments 1 and 2, each chick was fitted with a lens over one eye (randomly chosen), leaving the other eye uncovered. For experiment 3, both eyes were fitted with lenses. During experiments 2 and 3, in which birds wore negative lenses most of the day, the first brief episode of positive (or plano) lens wear was at the start of each day, with subsequent periods evenly spaced over the lights-on period of each day, ending with negative lens wear.

Measurements

Measurements of refractive error and ocular dimensions were conducted with chicks anesthetized with 1.5% halothane (Halocarbon Laboratories, River Edge, NJ). Refractive error was measured using a modified Hartinger refractometer (see Ref. 8 for details). A-scan ultrasonography with a 30-MHz transducer, sampled at 100 MHz, was used to measure internal ocular dimensions, specifically anterior chamber depth, lens thickness, vitreous chamber depth, and the thickness of retina, choroid, and sclera (see Ref. 9 for details). We defined ocular length as the sum of these components. It differs from axial length as used clinically, in that it includes the thickness of the retina, choroid, and sclera. Thus, increased choroidal thickness has no effect on the ocular length, but reduces axial length as conventionally defined. Birds were measured at the same time of day (between 10 AM and 2 PM) before and after the 3 days of lens wear. The second measurement was made approximately in the middle of one of the intervals between periods of positive lens wear.

Protocols

Treatments and lens-wearing paradigms for each experiment are listed in Table 1.

Experiment 1: Normal Vision Interrupted by Brief Periods of Monocular Lens Wear. To test the effects of very brief periods of monocular lens wear with normal vision the remainder of the day, some birds had 1 hour of +6 D lens wear per day, distributed in two, four, or six periods (groups 1 to 3; for group 1, the experiment was performed on two batches of birds, several months apart). Other birds wore +6 D, +10 D, or −15 D lenses for 12 minutes per day, distributed in six periods of 2 minutes (groups 4, 5 and 6, respectively). Lights went on immediately before the first period of lens wear and went off immediately after the last one.

Group 5 differed from the other groups, in that the viewing distance was fixed beyond the far point of the positive-lens–wearing eyes, allowing us to test whether brief periods of myopic blur could induce hyperopia in the absence of sharp vision. During lens wear, the chick was held in a container in the center of a drum. The drum had a radius of 30 cm, and the distances from the walls, the floor, and the lid of the drum were approximately the same, so that everything the bird could see was beyond the far point of its eye while wearing the +10 D lens (10 cm). This arrangement was similar to that used by Schaeffel and Diether.[10] The lids of the drums were made from translucent plastic that allowed light to enter the drum while preventing the chicks from looking out. To maintain the chicks' alertness, the chicks' containers were rotated by motors at a velocity of 30 deg/sec with the direction reversing every 30 seconds.

Experiment 2: Negative Lens Wear Interrupted by Brief Periods of Positive Lens Wear. To test whether brief periods of positive lens wear would induce hyperopia even when negative lenses were worn the remainder of the day, birds wore +6 D lenses monocularly for four daily periods of either 15 minutes (group 7) or 2 minutes (group 8), and wore −6 D lenses on the experimental eyes the remainder of the day. The fellow eyes were untreated. Two control groups wore −6 D and +6 D lenses continuously (groups 9 and 10, respectively).

Table 2. Summary of the Changes over (3) Days

		Refractive Error (D)			Vitreous Chamber Depth (μm)			Ocular Length (μm)			Choroidal Thickness (μm)		
Exp.	Group	Treated	Fellow	*P*	Treated	Fellow	*P*	Treated	Fellow	*P*	Treated	Fellow	*P*
1	1	1.7 ± 0.8	−0.3 ± 0.6	*	−16 ± 15	−7 ± 15	NS	68 ± 20	79 ± 21	NS	−47 ± 15	−57 ± 14	NS
		1.2 ± 0.6	0.1 ± 0.3	*	66 ± 24	75 ± 23	NS	163 ± 30	230 ± 25	†	−32 ± 17	−10 ± 10	NS
	2	2.8 ± 0.7	−0.7 ± 0.4	†	38 ± 28	155 ± 16	†	177 ± 29	253 ± 28	*	11 ± 18	−40 ± 25	NS
	3	2.3 ± 0.8	−0.6 ± 0.7	*	17 ± 27	159 ± 17	‡	168 ± 19	253 ± 21	†	6 ± 15	−84 ± 17	‡
	4	1.6 ± 0.5	0.2 ± 0.5	*	−17 ± 19	89 ± 22	‡	203 ± 18	272 ± 21	‡	32 ± 15	−4 ± 12	†
	5	1.3 ± 0.6	−0.8 ± 0.4	†	−21 ± 23	80 ± 16	†	91 ± 33	145 ± 28	NS	6 ± 21	−56 ± 16	NS
	6	0.5 ± 0.3	0.0 ± 0.3	NS	82 ± 15	95 ± 17	NS	122 ± 23	134 ± 20	NS	−73 ± 9	−82 ± 18	NS
2	7	2.9 ± 1.5	0.7 ± 1.0	*	−17 ± 24	109 ± 25	†	130 ± 26	242 ± 25	†	22 ± 11	−45 ± 11	†
	8	1.6 ± 0.8	−0.9 ± 0.6	*	49 ± 25	154 ± 35	*	234 ± 38	314 ± 35	NS	5 ± 22	−26 ± 16	NS
	9	−3.3 ± 0.7	0.3 ± 0.6	‡	273 ± 24	58 ± 27	‡	290 ± 53	179 ± 27	*	−75 ± 35	−7 ± 21	NS
	10	6.5 ± 0.7	−0.7 ± 0.6	‡	−176 ± 40	40 ± 23	‡	31 ± 40	144 ± 29	†	130 ± 28	−22 ± 18	†
3	11												
	+6 D	−1.8 ± 0.8		†	175 ± 28		‡	230 ± 32		‡	−86 ± 26		NS
	Plano	−3.4 ± 0.5			265 ± 23			316 ± 30			−88 ± 22		

In experiments 1 and 2, fellow eyes were untreated. In experiment 3, both eyes were treated simultaneously: one eye had brief periods of positive lens wear and the other eye had brief periods of plano lens wear, with both eyes wearing negative lenses the remainder of the day. Paired one-tailed *t*-tests were used except for groups 7 and 8, in which paired two-tailed *t*-tests were used. NS, not significant.

* $P < 0.05$.

† $P < 0.01$.

‡ $P < 0.001$.

Experiment 3: Binocular Negative Lens Wear Interrupted by Brief Periods of Positive Lens Wear on One Eye and Plano Lens Wear on the Other Eye. To compare in the same animals the protection afforded by positive lenses and the protection afforded by plano lenses against the myopia induced by negative lens wear, chicks wore −6 D lenses on both eyes all day, except for four periods of 2 minutes each day, during which one eye wore a +6 D lens, whereas the other wore a plano lens.

Statistics and Calculations

Data are shown as mean changes over 3 days, either for the treated and untreated eyes separately, or as the changes in the experimental eyes minus the changes in the fellow eyes ("relative changes"). For comparisons between two groups, we compared the relative changes of each group, by using unpaired, two-tailed *t*-tests; for three or more groups, we used analysis of variance (ANOVA) with Bonferroni post hoc tests.

To compare the effects of a treatment on one eye versus the fellow eye, we used paired *t*-tests. In experiment 1, for which one eye wore a positive lens and the other eye was untreated, we used one-tailed *t*-tests because we had a prior expectation that the lens-wearing eye would become hyperopic. For experiment 2, in which the experimental eye alternately wore negative and positive lenses (groups 7 and 8), there was no prior expectation about the direction of change, and therefore we used two-tailed *t*-tests. In experiment 3, in which binocular lens wear was interrupted by positive and plano lenses, our expectation was that either there would be no difference between the eyes or the positive lens–wearing eye would be less myopic, and therefore we used one-tailed *t*-tests.

Results

Brief periods of positive lens wear caused compensatory hyperopia, regardless of whether the birds had normal vision or negative lens wear the remainder of the time (experiments 1 and 2). Furthermore, if both eyes wore negative lenses, myopia was reduced more effectively by wearing positive lenses for brief periods than by wearing plano lenses for the same periods (experiment 3). The changes in refractive error, vitreous chamber depth, ocular length, and choroidal thickness over 3 days for all experiments are summarized in Table 2.

Experiment 1: Normal Vision Interrupted by Brief Periods of Monocular Lens Wear

Brief, Repeated Daily Periods of +6 D Lens Wear. Two to six periods of positive lens wear, totaling 1 hour per day, caused refractive compensation for the lenses (+1.1 D to +3.5 D shifts in the hyperopic direction relative to the shifts in the fellow eyes), despite normal vision in both eyes the remainder of the day (groups 1–3, Fig. 1A). When the total positive lens-wearing time was as little as 12 minutes (2 minutes six times per day, group 4), the lens-wearing eyes still showed a significant amount of compensation compared with fellow eyes (+1.6 D vs. +0.2 D, $P < 0.05$, paired one-tailed *t*-test). The relative changes (changes in experimental eyes minus the changes in fellow eyes) in refractive errors did not differ among the four groups ($P > 0.05$, ANOVA).

The refractive compensation that we observed was due mostly to inhibition of the deepening of the vitreous chamber, whereas the anterior segment length of the eye (and presumably the focal length of the cornea and lens combined) grew at a rate similar to that of normal eyes. (The increase in distance from cornea to the back of the lens did not differ between experimental eyes and either fellow eyes or age-matched normal eyes; ANOVA followed by the Bonferroni post hoc test, Fig. 1E.) In the groups wearing lenses more than twice daily (groups 2–4), the normal vitreous chamber growth was largely inhibited (6 μm increase over 3 days, compared with 127 μm in the fellow eyes), but the groups were not different from one another (Fig. 1B, Table 2). The group wearing the lenses only twice daily, which consisted of two batches of chicks hatched several months apart, showed no difference either time in the degree of vitreous chamber deepening between lens-wearing and untreated fellow eyes, despite a substantial, apparently idiosyncratic, difference in the degree of ocular growth between the two batches. (We occasionally found such batch-to-batch differences in the growth over several days, as have others.[11]) These birds showed significantly less inhibition of vitreous chamber deepening relative to fellow eyes than did

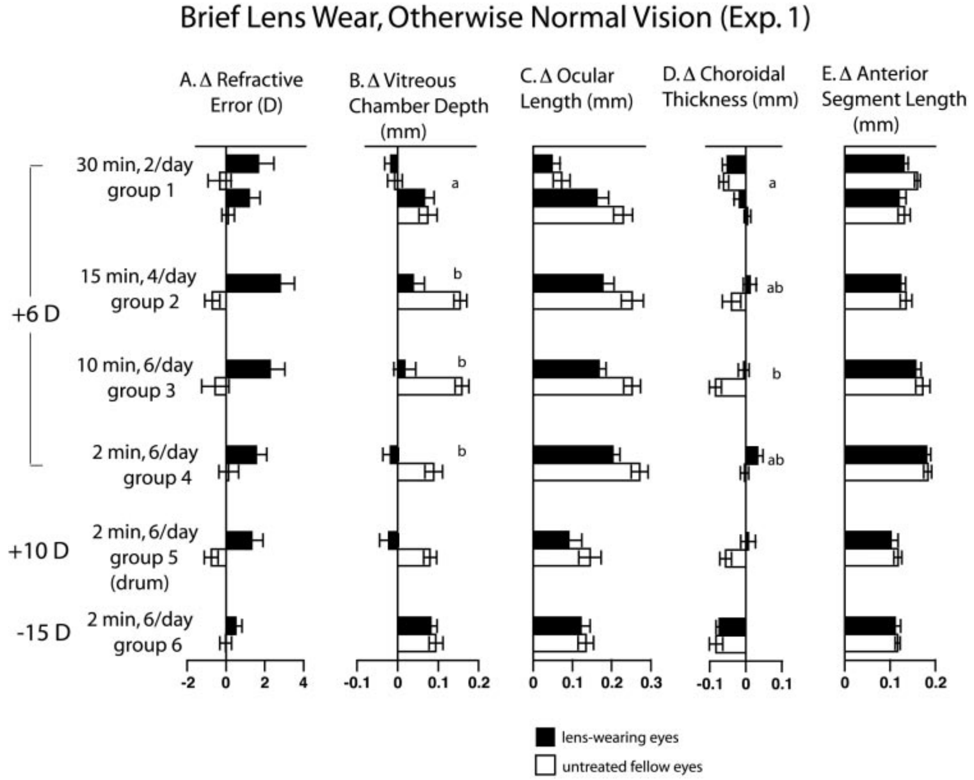

FIGURE 1. Changes over 3 days in refractive error (**A**), vitreous chamber depth (**B**), ocular length (**C**), choroidal thickness (**D**), and anterior segment length (the sum of anterior chamber depth and lens thickness) (**E**) of eyes with brief periods of +6 D, +10 D, and −15 D lens wear but with otherwise normal vision (experiment 1). Eyes wearing positive lenses became more hyperopic, with less vitreous chamber expansion and less ocular elongation than fellow eyes, whereas eyes briefly wearing negative lenses did not show any significant changes relative to the fellow eyes. The changes in the anterior segment length of the eye showed a similar pattern of growth in both experimental and fellow eyes. Error bars, SEM. The significance in the difference in "relative changes" (the changes in the experimental eye minus the changes in the fellow eye) in groups 1 to 4 was calculated using ANOVA with the Bonferroni post hoc test. Groups with different *lowercase letters* by each pair of bars differ significantly.

those with more lens-wearing periods each day ($P < 0.05$, ANOVA with Bonferroni post hoc test; data from two batches of group 1 combined). Overall, in 60 of 83 animals in groups 1 to 4, the vitreous chambers of the lens-wearing eyes grew less than those of the fellow eyes.

The inhibition of vitreous chamber deepening could have occurred either because the eye stopped elongating (and hence the vitreous chamber stopped deepening) or because the choroid thickened, thereby reducing the depth of the vitreous chamber. In the birds with four or six daily periods of lens wear (groups 2–4), the vitreous chamber deepened by 6 μm, compared with 127 μm in the fellow eyes. This 121-μm reduction in the deepening of the vitreous chamber was due more to slowed ocular elongation than to greater choroidal expansion (75 μm less ocular elongation than fellow eyes vs. 53 μm more choroidal expansion than fellow eyes across groups). In all four groups, the eyes wearing positive lenses elongated significantly less than their fellow eyes, except for one of the two subgroups of the 30-minute episode group (group 1, Fig. 1C). The relative changes in ocular length did not differ significantly among the four groups ($P > 0.05$, ANOVA).

The choroidal contribution that did exist was not a matter of absolute choroidal expansion, as occurs in birds wearing positive lenses continuously, but was due to less thinning than in the fellow eyes. The untreated fellow eyes of Truslow chicks of this age frequently had thick choroids (mean ± SD: 272 ± 86 μm, $n = 83$), which thinned over the next 3 days by 37 ± 67 μm, whereas the experimental eyes of groups 1 to 4 thinned only by 8 ± 68 μm. In general, the degree of thinning was greater in the eyes that started with thicker choroids (correlation of 0.72). In the case of the eyes briefly wearing positive lenses, this thinning was half as great (slope of 250 μm/mm of initial thickness in the experimental eyes vs. 520 μm/mm in the untreated eyes). This difference in slope is statistically significant ($P < 0.01$) by the algorithm of Edwards.[12]

Brief Positive Lens Wear with the Absence of Near Vision. To test whether the efficacy of the positive lenses was related to giving the eyes well-focused images (of near objects) or to giving the eyes myopic defocus (of more distant objects), we fitted birds with +10 D lenses on one eye for 2 minutes six times a day, only when they were restrained in the center of a drum (group 5). Because the walls of the drum were 30 cm (3.3 D) from the chick, and the lens-wearing eyes had refractive errors of −0.8 ± 1.5 D (mean ± SD) at the start of the experiment, the eyes would have experienced an average of 7.5 D of myopic blur without accommodation, or possibly as little as 3.5 D of myopic blur, if they negatively accommodated by the maximum shown by Troilo et al. (Troilo D, Li T, Howland HC, ARVO Abstract 2990, 1993). (Elsewhere,[13] we have reported that the degree of compensation in the drums is not related to the starting refractive error.)

The birds briefly wearing positive lenses in the drums showed consistent, significant compensation, both in refractive error (Fig. 1A) and vitreous chamber depth (Fig. 1B). The relative changes in refractive error and in vitreous chamber depth did not differ significantly from those of birds in group 4, which had the same lens-wearing schedule but were unrestrained in their cages wearing +6 D lenses ($P > 0.05$, unpaired 2-tailed *t*-tests). Thus, the response to positive lenses was not strongly affected by the absence of sharply focused images. (We fitted the chicks' eyes with +10 D lenses in the drums to ensure that they experienced only myopic defocus. We compared them with birds wearing +6 D lenses in their cages, because if they were viewing distant objects, these lenses would approximate the degree of defocus that the drum-enclosed chicks experienced. The chicks in the cages probably experienced less defocus, because of the availability of nearby objects. In other work,[13] we have shown that there is no difference between the effect of wearing +10 and +6 D lenses in the drum.)

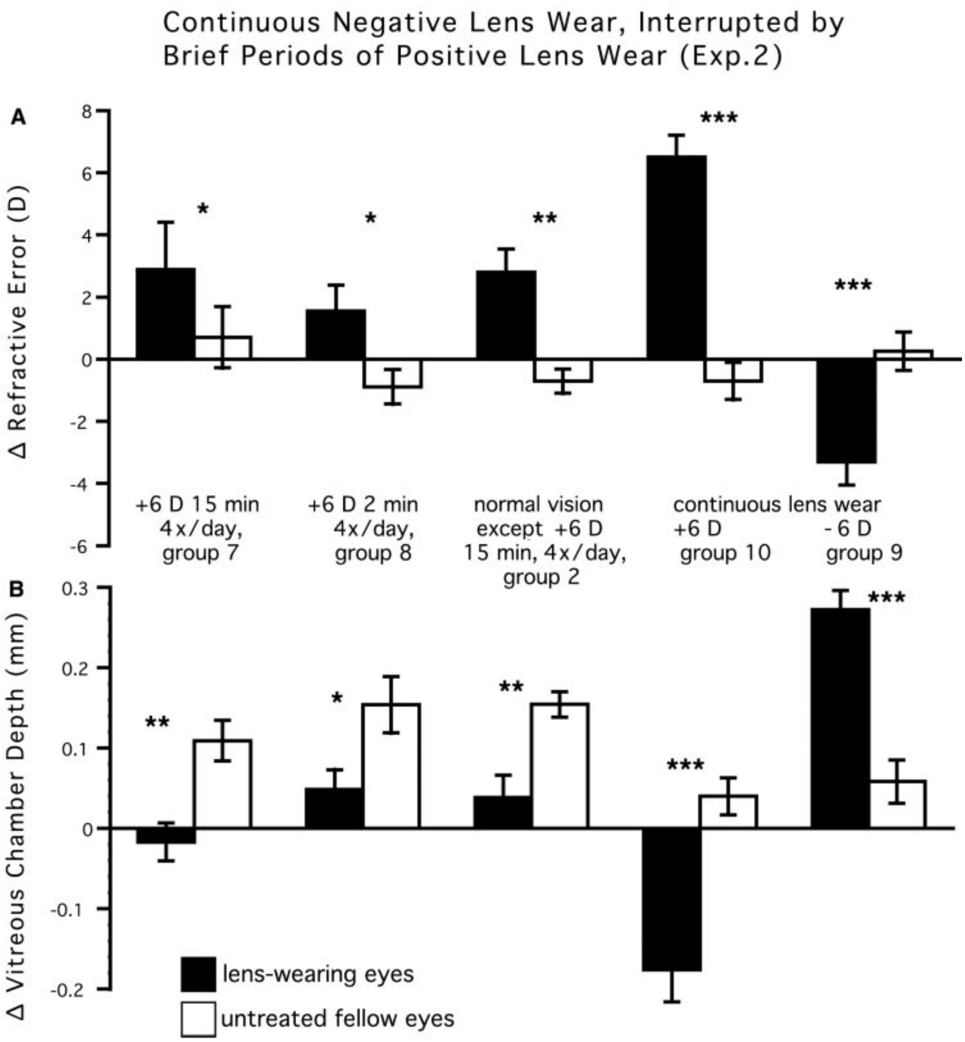

FIGURE 2. Changes in refractive error (**A**) and vitreous chamber depth (**B**) for negative lens wear interrupted by brief periods (15 or 2 minutes) of positive lens wear (experiment 2). In both groups, hyperopia developed in the experimental eyes, and vitreous chamber elongation was inhibited. For comparison, eyes with brief periods of positive lens wear with normal vision the remainder of the day and continuous positive or negative lens wear are shown on the *right*. The response to brief periods of positive lens wear is similar, regardless of whether the eye had normal vision or negative lens wear the remainder of the day. (In the continuous lens wear groups the vitreous chamber deepened less than normally occurs.) Error bars, SEM. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$, paired two-tailed *t*-test for groups 7 and 8, paired one-tailed *t*-test for groups 2, 9, and 10.

Brief Periods of Negative Lens Wear. To examine whether brief periods of negative lens wear could also induce compensation, birds were fitted with −15 D lenses for 2 minutes six times per day (group 6), the same schedule used for groups 4 and 5, which was the least amount of lens wear used that induced significant compensation for positive lenses. In contrast to positive lenses, negative lenses briefly worn did not cause compensatory changes in refractive error, vitreous chamber depth, ocular elongation, or choroidal thickness (Figs. 1A–D).

Experiment 2: Negative Lens Wear Interrupted by Brief Periods of Positive Lens Wear

As expected, wearing negative lenses continuously for 3 days caused eyes to develop myopia (−3.3 D) and a substantial increase in vitreous chamber depth (Fig. 2, Table 2). Interrupting this negative lens wear with positive lenses four times a day for either 15 or 2 minutes not only prevented the development of myopia but also caused the eyes to become significantly hyperopic, despite the preponderance of negative lens wear (+2.3 D, Fig. 2A, groups 7 and 8, $P < 0.05$, paired two-tailed *t*-test). Thus, the eyes briefly wearing positive lenses became approximately 5.5 D more hyperopic than they would have been had they worn only negative lenses. These effects were consistent: In 12 out of 16 birds in the two groups, the lens-wearing eyes shifted more toward hyperopia than their fellow eyes.

The refractive shifts were accompanied by significant changes in vitreous chamber depth. Positive lenses either entirely halted (group 7, 15-minute periods) or reduced by two thirds (group 8, 2-minute periods) the increase in vitreous chamber depth shown by the untreated fellow eyes, with both amounts of change significantly less than that of the fellow eyes (by two-tailed *t*-tests). The inhibition was greater in the 15-minute group than in the 2-minute group (group 7 vs. group 8, $P < 0.05$, unpaired one-tailed *t*-test). Across the two groups, 13 of 16 lens-wearing eyes had vitreous chambers shorter than the fellow eyes.

Even if the amount of vitreous chamber expansion had been identical in the lens-wearing and the fellow eyes, this would have represented a powerful effect of the brief wearing of positive lenses, because negative lens wear alone would more than double the normal rate of vitreous chamber expansion (group 9, Fig. 2B). In fact, the brief wearing of positive lenses eliminated the 300 μm of vitreous chamber elongation shown by the birds wearing only −6 D lenses (compare first two solid bars in Fig. 2B with last solid bar) and caused the elongation rate to be even slower than in the fellow, untreated eyes.

Therefore, 1 hour or less of positive lens wear had a stronger effect than 11 hours or more of negative lens wear, in terms of both refractive error (Fig. 2A) and vitreous chamber depth (Fig. 2B). In fact, the resultant hyperopia and vitreous chamber inhibition in experimental eyes was as great as in the birds that

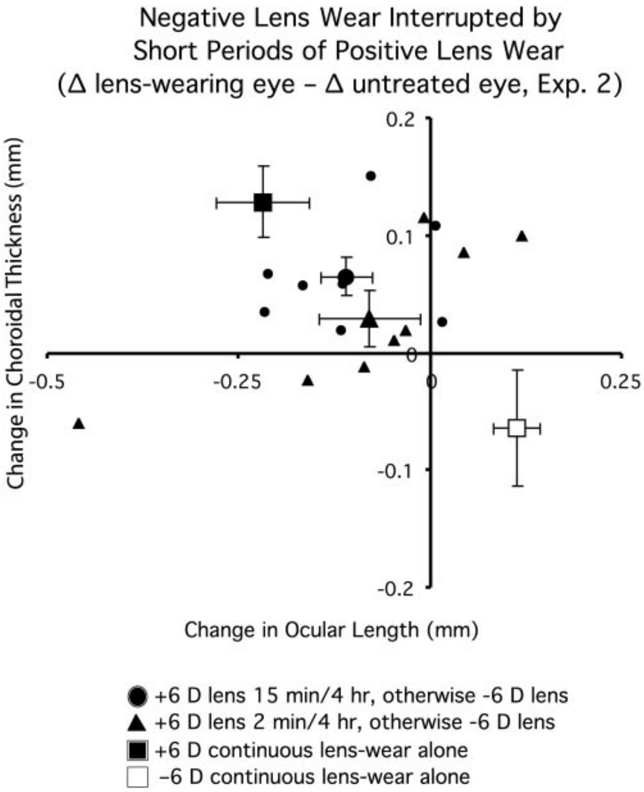

FIGURE 3. A scatterplot of effects on choroidal thickness and ocular length of negative lens wear interrupted by brief periods of positive lens wear. The values plotted are the changes over 3 days in treated eye relative to those in untreated fellow eyes. *Small symbols*: individual data; *large symbols*: means. For comparison, mean results are also shown for continuous positive and negative lens wear. Most of the birds with brief periods of +6 D lens wear had slowed axial elongation and thickened choroids relative to the fellow eye (*top left quadrant*). Error bars, SEM.

wore no lenses between the periods of positive lens wear (group 7 vs. group 2, $P > 0.05$, unpaired one-tailed *t*-test; Fig. 2).

The inhibitory effects of the brief periods of positive lens wear on the vitreous chamber depth were due both to a reduced rate of ocular elongation and an increased choroidal thickness, compared with the fellow eyes. When the positive lenses were worn for either 15 or 2 minutes four times a day (groups 7 and 8), the total ocular length increased by two thirds as much as in fellow eyes (Table 2), and the choroids thickened slightly, whereas the choroids in the fellow eyes thinned (Fig. 3). To see the full effect of briefly replacing the negative lenses with positive lenses, we can compare the responses of the positive lens-wearing eyes to the responses of the eyes with continuous negative lens wear (group 9). Ocular elongation was much slowed (−112 μm vs. +111 μm, group 7 vs. group 9), and choroids were much thicker (+67 μm vs. −68 μm; Table 2, Fig. 3), relative to the untreated fellow eyes. Finally, both the ocular length inhibition and the choroidal expansion in experimental eyes were greater in the 15-minute group than in the 2-minute group ($P < 0.05$, unpaired one-tailed *t*-test).

Experiment 3: Binocular Negative Lens Wear Interrupted by Brief Periods of Positive Lens Wear on One Eye and Plano Lens Wear on the Other Eye

To assess how much of the canceling of the negative lens-compensation myopia that we observed is specific to wearing positive lenses, we compared in the same animal the effect of replacing negative lenses with four 2-minute periods of positive lenses on one eye and plano lenses on the other eye (group 11). Brief positive lens wearing attenuated the negative lens response significantly more than did brief plano lens wearing. Specifically, the eyes wearing positive lenses became about half as myopic as eyes wearing plano lenses (−1.8 D vs. −3.4 D, $P < 0.01$, paired one-tailed *t*-test; Fig. 4A), with a one-third reduction in both vitreous chamber expansion and ocular elongation (vitreous: 175 μm vs. 265 μm, $P < 0.001$; ocular elongation: 230 μm vs. 316 μm, $P < 0.001$). These changes were consistent: In 11 of 13 birds, the positive lens-wearing eyes became less myopic, and in 12 of 13 birds the positive lens-wearing eyes had less-elongated vitreous chambers than the plano lens-wearing eyes (top left quadrant in Fig. 4B). Neither treatment had a significant effect on choroidal thickness (Fig. 4A).

When negative lenses were briefly replaced by positive ones, eyes shifted toward hyperopia and showed inhibited vitreous chamber deepening, regardless of whether the negative lenses were worn over one eye (experiment 2) or both eyes (experiment 3). However, the two eyes did not act entirely independently. If negative lenses were worn over both eyes, they had a greater effect than if worn over one eye, in that both eyes were more myopic and had thinner choroids. This additional myopia both made the eye briefly wearing a positive lens myopic (although less so than the eye briefly wearing a plano lens) and made the eye briefly wearing a plano lens as myopic as an eye wearing a negative lens continuously, with the other eye normal (group 11 vs. group 9: −3.4 D vs. −3.3 D; $P > 0.05$, unpaired two-tailed *t*-test, Figs. 2A, 4A).

DISCUSSION

We have shown that, in chicks, wearing a positive lens for brief periods (totaling 12 minutes to 1 hour per day) caused substantial compensation in the hyperopic direction, even if the eye wore no lens or a negative lens the remainder of the day. More protection against the myopia caused by negative lens wear was exerted by wearing positive lenses than by wearing plano lenses. These results dramatically extend the finding that if positive and negative lenses are worn in alternation, the compensation is in the direction of the positive lenses.[6]

Compensatory Hyperopia Caused by Brief, Repeated Periods of Positive Lens Wear

As little as 12 minutes a day of positive lens wear caused compensation in the hyperopic direction, despite normal vision the remainder of the day. This compensation occurred even if the birds had only a myopically blurred view of their surroundings by wearing positive lenses only when restrained in a drum, the walls of which are beyond the far point of the eyes. These results suggest that the myopically defocused images have a stronger effect than the images that the bird sees the remainder of the day while in the cage, thereby extending the results of Park et al.[13] obtained with birds kept in the dark between lens-wearing sessions in the drum. Our results also extend the findings of Schmid and Wildsoet[7] that positive lenses produce compensation even if worn for 3 hours once a day, with normal vision the remainder of the day. That we got consistent compensatory responses to such a small amount of lens wear is probably because the lens wear was broken up into multiple periods. We found that six periods of 2 minutes each yielded significantly better compensation than two 30-minute periods, and six periods of 10 minutes each showed a (nonsignificant) trend toward even better compensation. These differences are consistent with previous findings that

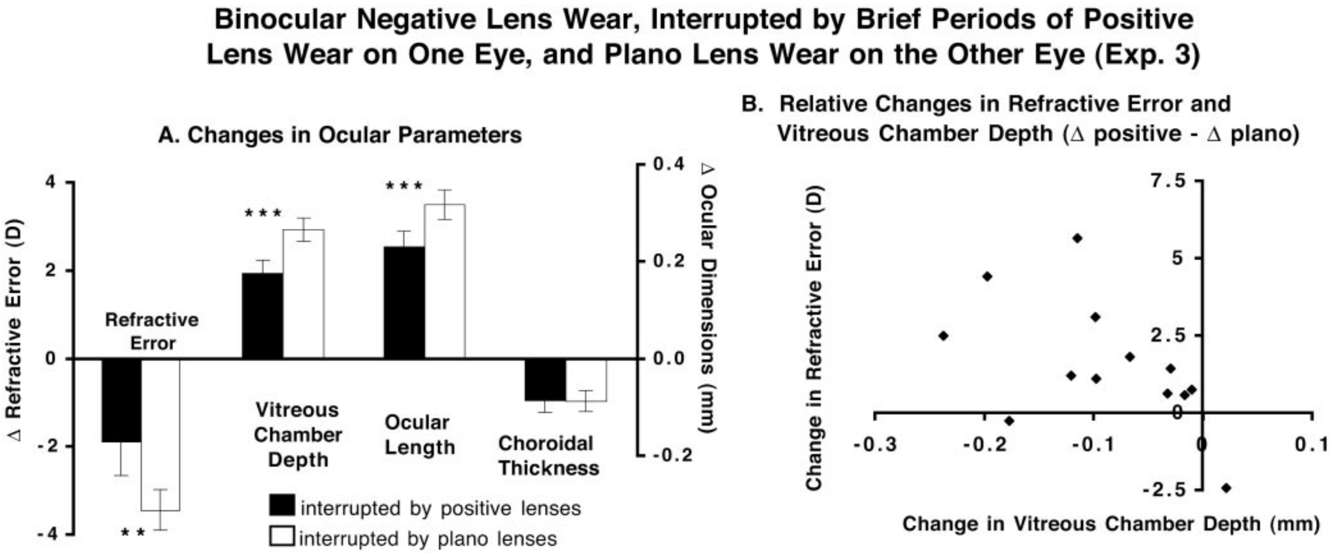

FIGURE 4. Changes over 3 days of binocular negative lens wear interrupted by brief periods of positive lens wear on one eye and plano lens wear on the other eye (experiment 3). (**A**) Briefly worn positive lenses attenuated the negative-lens responses more than did briefly worn plano lenses. The two eyes are shown separately. Error bars, SEM. (**B**) The interocular difference between the effects of positive and plano lens wear in individual animals in refractive error against vitreous chamber depth (relative changes: the changes in the positive lens-wearing eyes minus the changes in the plano lens-wearing eyes). Most of the birds both changed more in the hyperopic direction and had less vitreous chamber expansion in the positive lens-wearing eye than in the plano lens-wearing eye (*top left quadrant*). $^{**}P < 0.01$, $^{***}P < 0.001$, one-tailed paired *t*-test.

brief, repeated periods of positive lens wear cause better compensation than a single long period (chicks in darkness between lens-wearing periods), although that compensation decreases if individual periods are shorter than a few minutes in duration.[6] Similarly, Napper et al.[14] found that removing diffusers (which induce form-deprivation myopia when worn continuously) for 10 minutes 3 times a day prevented myopia better than did removing them for a single daily period of 30 minutes. These findings are also consistent with those of Kee et al. (Kee C-S, Hung L-F, Qiao Y, Ramamirtham R, Winawer JA, Wallman J, Smith EL, ARVO Abstract 2925, 2002), which showed that replacement of negative lenses with plano lenses for 15 minutes, four times per day, completely prevented development of myopia in monkeys, whereas replacement of diffusers with plano lenses for one period of 60 minutes per day reduced myopia by approximately 50%.[15]

Compensatory Hyperopia Despite Daylong Negative Lens Wear

Surprisingly, briefly worn positive lenses were equally effective in inducing hyperopia, whether the birds wore negative lenses or no lenses the remainder of the day (groups 2 and 7, Fig. 2); both groups wore positive lenses for 15 minutes, four times per day and shifted by 2.8 and 2.9 D, respectively, in the hyperopic direction. This result seems less surprising if we consider that at this point, because the eyes had half-compensated for the positive lenses, both groups would have experienced hyperopic blur most of the day whether or not they wore negative lenses, and both groups would have experienced a similar degree of myopic blur when wearing the positive lenses. Of course, the eyes wearing negative lenses would be experiencing more hyperopia because the negative lenses would add to their own refractive error. The similar progression in both cases implies that both degrees of hyperopia have similar effects. This similarity is consistent with the finding that the rate of lens compensation when lenses are first fitted is similar for lenses of different strength, implying that it is the sign, more than the power, of the lens that drives lens compensation (Wildsoet C, Wallman J, ARVO Abstract 2152, 1997).

If negative lenses are worn all day, simply replacing them with plano lenses for brief periods is less effective in preventing myopia than replacing them with positive lenses. Although the average refractive error at the start of our experiments was small (mean ± SD: positive lens-wearing eyes = 0.3 ± 0.5 D, plano lens-wearing eyes = 0.2 ± 0.3 D), individual eyes varied considerably. Therefore, in some cases, replacing the negative lens with the plano lens would have simply reduced the amount of hyperopia, whereas in others it would have presented myopic defocus, especially as the experiment went on and the negative lenses exerted their effects. Presumably the stronger and more consistent myopic defocus imposed by the +6 D lenses explains their more potent inhibition of myopic progression. Thus, it seems clear that it is the presence of the positive lens that is particularly effective in canceling the compensation for negative lenses, rather than the absence of the negative lens. In contrast, in a similar experiment on monkeys, replacing a negative lens with plano lens was more effective than replacing it with a +4.5 D lens (Kee C-S, Hung L-F, Qiao Y, Ramamirtham R, Winawer JA, Wallman J, Smith EL, ARVO Abstract 2925, 2002), perhaps because too much myopic defocus was imposed by the positive lens, especially once the eye became myopic, for good compensation (+4.5 D is near the limit of compensation, according to Smith and Hung[16]).

In our experiment with monocular negative lens wear (experiment 2), we found that brief periods of positive lens wear caused hyperopia, despite negative lens wear the remainder of the day, whereas in our binocular experiment (experiment 3), the same condition led to a small amount of myopia. We infer from this that binocular negative lens wear causes more myopia than does monocular negative lens wear; the same has been shown for form-deprivation myopia.[11] Such interocular yoking effects have been reported before in chicks,[7,11,17] monkeys,[4] and guinea pigs (McFadden S, Wallman J, ARVO Abstract 3504, 1995).

Myopic Defocus Protects against Myopia

We have shown that briefly wearing positive lenses can prevent the myopia that would otherwise have resulted from wearing negative lenses. This protective effect may arise, either because the positive lenses increase the amount of myopic defocus or because they reduce the overall level of defocus that chicks experience, by bringing nearby objects into focus. We argue that the former explanation—increasing myopic defocus—is more likely. When chicks had myopic vision imposed by wearing +10 D lenses only when inside a large drum (with normal vision the remainder of the day), vitreous chamber deepening halted and the eyes became more hyperopic. Others have also found compensation for positive lenses in similarly restricted environments, either when a similar degree of myopic defocus is presented continuously (Diether S, Wildsoet CF, ARVO Abstract, 2002), or when the myopic defocus was presented for brief periods several times per day while the chicks were otherwise kept in the dark.[10,13] Furthermore, when both myopic and hyperopic defocus were presented simultaneously, either by means of Jackson-crossed cylinder lenses[18] or by multifocal spherical lenses (Wildsoet CF, Collins MJ, ARVO Abstract 3930, 2000) the effects of myopic defocus predominated. In contrast, a recent abstract using methods similar to those of Diether and Wildsoet found no compensation for myopic defocus greater than +2 D (Schmid KL, Iskander DR, Brinkworth D, Ainsworth T, ARVO Abstract 187, 2002).

The very brief periods during which our chicks wore positive lenses makes it unlikely that their efficacy is due to decreasing the average degree of defocus the chicks experienced. It is difficult to see why 12 min/d of sharp vision should switch the refractive status from myopic to hyperopic, given that the birds had the remainder of the day to accumulate sharp vision by means of accommodation.

Thus, although myopia can be caused either by diffusers,[8,19–21] negative lenses,[1–3] or very strong positive lenses,[22] within a range of powers, positive lenses can strongly counteract the effect of negative lenses, probably by imposing a degree of myopic blur. It is unknown what the visual cues are that distinguish the blur that protects against myopia from the blur that causes it.

Clinical Implications

The finding that myopic blur reduces myopia has several possible clinical implications. First, it suggests that maximizing the sharpness of the retinal image may not be the best prophylaxis for myopia. Second, it suggests that transient myopia caused by hysteresis of accommodation, in which accommodation does not immediately relax after a long period of nearwork, may not be a cause of myopia, as has been previously suggested.[23,24] On the contrary, our findings suggest that a little manifest myopia whenever one looks up from reading might counteract the effect of the preceding long period of hyperopic defocus resulting from the nearness of the page and the lag of accommodation. Perhaps those children who read as much as their myopic siblings but do not become myopic are ones who look up from the page often enough to counter the effect of the nearwork, possibly aided by a high level of transient myopia. But of course we know nothing about the amount of time or the distribution of periods of distant vision that would counter the effect of reading in children.

Third, that myopic defocus cancels the effects of hyperopic defocus suggests a reason that the eye may be more predisposed to myopia by reading than by other forms of nearwork. Under natural conditions, near vision would generally involve the examination of small objects against a distant (hence myopically defocused) background. Our results suggest that the presence of myopic blur protects against the development of myopia. During reading, however, the myopically defocused distant contours are blocked by the page, thereby potentiating the myopigenic effect of the hyperopic defocus caused by the nearness of the page. It has been shown in chicks that a near target causes less myopia if the chick can see distant objects behind the target than if the target is the only visual stimulus.[25]

Relation to Progression of Myopia in Humans

If myopic defocus in humans is as potent a counterforce to myopia as it is in chicks, it seems that myopia would be a self-limiting condition, rather than one that progresses for years. One long-standing view is that, if uncorrected, myopia would quickly reach an asymptote, but that the optical correction of myopia by negative lenses prevents this from occurring by restoring the original myopiagenic conditions (i.e., hyperopic defocus). Although this idea has not been adequately tested, one study involving few subjects suggests that the course of myopic progression can be slightly better fitted by assuming that progression is more rapid just after corrective spectacles are replaced by stronger ones.[26]

More generally, one might expect that whenever a myopic eye is undercorrected, any distance vision would contribute myopic defocus, which would slow the myopic progression. In two studies, it was found that under- or uncorrected myopia progresses at half or two thirds the rate as fully corrected myopia, but the number of subjects in each study was small, and the results were complicated by other factors (Tokoro and Kabe[27] and Ong et al.[28]). In a larger study (Roberts and Banford, as reported by Goss[29]), the effect of undercorrection was negligible, but the degree of undercorrection present was very small. In a recent study of 94 children, myopes with refraction undercorrected by 0.75 D progressed more rapidly than those whose refraction was fully corrected.[30] Thus, this issue is unresolved at present.

There are, in addition, studies of the effects of bifocals and of progressive addition lenses on myopic progression. Some studies show that bifocals reduce myopic progression[31–32]; others show no effect.[33–35] Three studies of progressive lenses, including one large multi-center trial, showed a modest reduction in myopic progression,[36–38] with a greater efficacy in children with weak accommodation.[38] The most consistent finding is that bifocals reduce myopic progression in children with esophoria at near (reviewed by Goss[29]). These findings, in contrast to those in chicks, point to the complex influence of binocular factors in the progression of myopia in children, especially as it might be the case that much of the accommodation is vergence-accommodation rather than blur-driven accomodation. If this is the case, it would be difficult to infer from measurements of blur-driven accommodation how much blur would be experienced during reading; direct measurements are needed. These binocular interactions argue for caution in extrapolating from chicks to children.

Possible Differences between Chicks and Children

As discussed in the previous section, it is uncertain whether myopic defocus prevents myopia in children. If it does not, what might account for the potent effects of myopic defocus in chicks? One possibility is that the strong protective effect of positive lenses shown in the current study is specific to the neonatal period and declines subsequently. Thus, these effects would be relevant to the early emmetropization period in humans during the first year or two of life, not to the period when most "school myopia" develops. A second possibility is that the levels of myopic defocus that children experience as a result of the under-correction (either deliberately or because of changes in refractive state between fittings of spectacle corrections) are not sufficient to exert a protective effect. Because chicks compensate for much higher powers of positive lenses than do monkeys and because the experiments reported herein all used rather high-powered positive lenses (+6 D and +10 D), until a range of positive lens powers is tested in monkeys, we cannot confidently extrapolate our results to children.

A third possibility is that the protective effects of positive lenses exist only in chicks and not in humans. We regard this as unlikely, in light of the similarly large reductions in myopia in monkeys,[15] tree shrews,[39] and chicks[7,40] when negative lenses or diffusers are removed for 1 hour each day,[15] suggesting that the underlying mechanisms are evolutionarily well conserved. Because the manifest myopia during the 1 hour without lenses or diffusers balanced the 11 hours or so of negative lens wear or diffuser-wear across species, we expect that the protective effect of positive lenses will be found in other species.

However, the details of the temporal characteristics of the effect of positive lenses may well differ dramatically among species. The conditions just discussed, of negative lenses or diffusers worn all day except for one block of 30 minutes of myopic vision, are unlikely to be experienced by either chicks or children living normally. In other studies as well as this one (Fig. 1), we have shown that the amount of compensation for positive or negative lenses depends as much on the frequency and duration of the lens wear as on the total amount of lens wear. Specifically, frequent periods of lens wear are more effective than the same amount of lens wear in single daily doses[6]; very brief periods of lens wear are ineffective, regardless of their frequency[6]; and the effect of alternating positive and negative lenses depends on the frequency of alternation (Zhu X, Winawer JA, Choi JW, Wallman J, ARVO Abstract 2929, 2002) and cannot be predicted from the effects of the same duration of wear of each lens.[6] To apply these results to children would necessitate knowing the temporal distribution of periods of reading, as well as the amount and sign of blur experienced during reading and other near work. Such knowledge of the natural patterns of blur experienced by developing animals or children might lead to quantitative models of the dynamics of emmetropization, which could greatly improve our ability to understand the link between nearwork and myopia.

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