Normal Emmetropization in Infants with Spectacle Correction for Hyperopia

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PURPOSE. The development of emmetropic refraction is known to be under visual control. Does partial spectacle correction of infants' refractive errors, which has been shown to have beneficial effects in reducing strabismus and amblyopia, impede emmetropization? The purpose of the present study was to perform the first longitudinal controlled trial to investigate this question in human subjects.

METHODS. Children identified as having significant hyperopia in a population screening program at age 8 to 9 months were assigned to treated (partial spectacle correction) or untreated groups. A control group of infants with no significant refractive errors at screening was also recruited. Measurements of retinoscopic refraction under cycloplegia were taken at 4- to 6-month intervals up to the age of 36 months, and changes in refraction of 148 subjects were analyzed longitudinally.

RESULTS. Refractive error decreased toward low hyperopic values between 9 and 36 months in both hyperopic groups. By 36 months, this reduction of hyperopia showed no overall difference between children who were treated with partial spectacle correction and those who were not. Despite the improvement, both hyperopic groups' mean refractive error at 36 months remained higher than that of the control group. When infants in all three groups were considered together, the rate of reduction of refractive error was, on average, a linear function of the initial level of hyperopia.

CONCLUSIONS. The benefits of spectacle correction for infants with hyperopia can be achieved without impairing the normal developmental regulation of refraction. (Invest Ophthalmol Vis Sci. 2000;41:3726–3731)

A significant proportion of infants show hyperopia of more than +3.5 D.1,2 In a large-scale photorefractive screening program,1 we detected such infants and followed them up longitudinally, alongside a control group without significant refractive error. We have already reported that partial spectacle correction of hyperopia in infancy is of significant benefit, in that compared with uncorrected hyperopes, those who wore a correction showed better acuity for single and crowded letters, and a lower incidence of strabismus, at 4 years of age.3,4 However, we wanted to examine whether this correction also affects the normal reduction of hyperopia during early life. In the current study we investigated emmetropization in the same group of infants, comparing hyperopes who were prescribed spectacles with those who were not given correction.

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The mechanisms that regulate human ocular development are poorly understood. Pioneering studies of other animals including primates5–9 have suggested that ocular development and refraction are partly regulated by visual feedback related to optical defocus. Making chicks artificially myopic using plus lenses produces compensatory ocular growth6,10 that can eliminate the refractive error. However there has been some controversy about the extent of these effects in mammals, for both hyperopic and myopic defocus, and their application to human development.11–17 Refraction in human infants is usually hyperopic, and generally develops gradually toward emmetropia during the first years of life.18–21 However, the extent to which defocus or accommodation induced by lenses may affect this process has not yet been resolved. In particular, there have been no studies to date comparing human emmetropization in matched groups of infants with corrected and uncorrected refractions who have hyperopic refractive errors. The purpose of the present study was first to examine refractive changes between the ages of 9 months and 3 years in human infants who had naturally occurring hyperopic refractions and compare them with infants with normal refractions, and second to compare changes in refraction in infants with hyperopia who were given correcting spectacles with changes in those who did not receive correction. We present results for three groups: infants who were significantly hyperopic at 9 months and were treated with partial spectacle correction (n = 44), infants who were significantly hyperopic at 9 months and were not treated (n = 37), and a control group with normal refraction at 9
months \((n = 36)\). A further analysis examines the change in refraction of the subgroup of treated infants who consistently wore the prescribed correction.

**METHODS**

**Population of Infants in this Study**

Children born in the central area of the Cambridge Health District (Cambridgeshire, UK) during a 2.5-year period in 1981 through 1983 were invited to attend vision screening appointments in well-infant clinics. A total of 3166 infants (74% of those invited) attended this population-based community screening program.\(^1\)\(^-\)\(^3\) Screening took place at 7 to 9 months of age and included an orthoptic examination and cycloplegic photorefraction (isotropic photorefractor on 35-mm camera, \(^4\) with 1 to 2 drops of 1% cyclopentolate administered 30 to 40 minutes before photorefraction). The procedure for photorefraction, its theoretical rationale, and validation against retinoscopy have been described in previous publications.\(^1\)\(^-\)\(^3\)\(^2\)\(^2\)\(^3\) The hyperopic groups consisted of infants identified at screening with at least one meridian of +3.5 D or greater, confirmed by a retinoscopic examination in eyes under cyclopia at a follow-up examination within 45 days of screening. This procedure confirmed significant hyperopia, according to the criterion of at least one meridian of +3.5 D or greater, in 89% of infants deemed to have hyperopia at screening. The first infant to be screened without hyperopic, anisometric, or myopic refraction (see Reference 1 for criteria) after an infant with refraction categorized as hyperopic at screening was recruited as part of the control group and comprised a random sample of the infants who did not meet the criteria for the refractive error categories. Refractions of control infants were also confirmed by cycloplegic retinoscopy. The goal was to obtain a control group of approximately 50% of the study population. Infants with diagnosed developmental delay were not included in this study. Children in the trial were offered appointments at 4- to 6-month intervals, at which a range of measures of visual development were made. In the present study, we describe only changes in retinoscopic refraction under cyclopia across these follow-up visits.

The research protocol adhered to the Declaration of Helsinki for research involving human subjects. All parents or guardians of the infants studied provided written consent to the screening and follow-up assessments.

**Spectacle Correction and Compliance**

Infants identified as having significant hyperopia but with no meridian greater than +6 D, were alternately assigned to the treated or untreated groups. For infants treated in the trial, spectacles were prescribed according to the following protocol:

- **Sphere:** 1 D less than the least hyperopic meridian (corrections under 1.5 D were not prescribed)
- **Cylinder:** up to 2 years of age, half of any astigmatic error if over 2.5 D; 2 to 3.5 years, half of any astigmatic refractive error; more than 3.5 years, full correction.

This protocol was adopted to ensure that astigmatic errors, which are known to reduce rapidly in infancy,\(^2\)\(^4\) did not become overcorrected during the period between follow-ups and that some accommodative demand remained, similar to that for an infant with average refraction of +1.0 D to +1.5 D. If at any follow-up visit refractive error had reduced below these criteria, the spectacle correction was discontinued, but the child was retained as part of the treated group for analysis.

A questionnaire at each follow-up asked parents what proportion of waking time the child had worn glasses in the current period. Every effort was made to encourage parents to provide honest answers and not to exaggerate the periods of spectacle wear. Infants with reported spectacle wear of 50% or more waking time were classified as compliant. Changes in refraction were initially analyzed according to intention-to-treat, but the data were also reanalyzed with those subjects who did not meet the criterion for compliance excluded from the treated group. The former analysis respected the original alternate assignment, whereas the latter served to evaluate more specifically the optical effect of correction.

**Longitudinal Analysis**

At screening, 208 of the 3166 infants (6.6%) met the criterion for hyperopia. Of these, 199 (96%) who attended the follow-up appointment and had cycloplegic retinoscopy, 177 (89%) were confirmed hyperopic (at least one meridian of more than +3.5 D), but in the present analysis, we considered only the 148 infants who had a meridian of more than +3.5 D.

Infants with any meridian more than +6 D \((n = 18)\), anisometropia more than 1.5 D between parallel meridians \((n = 5)\), or manifest strabismus \((n = 1)\) were referred for immediate appropriate ophthalmic treatment and were not included in the trial of refractive correction. (One child’s condition fit two of these diagnostic categories.) Of the remaining 125, the intention-to-treat group comprised 62 infants, whereas the no-intention-to-treat group comprised 63. An outcome measure taken between ages 24 and 36 months was available for 46 infants in the intention-to-treat group (74% of those entering the group) and 43 in the no-intention-to-treat group (68%). Of those lost to the study between 9 and 36 months, 18 had development of a visual problem that met the criteria for referral for ophthalmic treatment, and they did not subsequently attend the follow-up visits reported in this study. The remaining 18 moved from the area, failed to attend, or attended but were uncooperative during attempted retinoscopy.

In the control group, 106 of the 162 infants (65%) recruited at screening had cycloplegic retinoscopy at 9 months; 105 of these (99%) were confirmed to have all meridians below +3.5 D. An outcome measure is available for 59 infants (56%). The higher rate of withdrawal in this group was mainly due to failure to attend. Presumably, their parents perceived less benefit of attendance than did those who had children with hyperopia.

To provide a more detailed picture of refractive development, our primary analysis considered the infants for whom, in addition to an initial and final retinoscopy measure, we had obtained an intermediate measure between 16 and 24 months. This reduced our groups to 44 intention-to-treat hyperopes (71%), 37 no intention-to-treat (59%), and 36 control subjects (34%), totalling 53 boys and 64 girls. A subsidiary longitudinal analysis considering only the initial and final measures was also performed.

If more than one refractive measure was available for an infant at the intermediate ages, the earliest available measure was used for the analysis; whereas for the outcome, the last available measure was used.
Statistics

Treated and untreated infants were compared on measures of hyperopia and astigmatism, using repeated-measures analyses of variance with age as a within-subjects factor, and treatment and gender as between-subjects factors. The initial (9 month) values were used as covariates to remove any effects due to small differences in the distributions of initial refractions between the two groups. For assessments of outcome, independent samples t-tests were used to compare the final (36 month) means. In addition, linear regression analyses were performed to determine the relation between initial hyperopia or astigmatism and change over the course of the study.

RESULTS

Emmetropization

Figure 1 plots the mean level of hyperopia for each group over the course of the study period, taking for each infant the single meridian of the four (two for each eye) most hyperopic at each measurement. The initial means (±SD) were +1.9 ± 0.8 D in the control group, +4.6 ± 0.5 D in the treated hyperopic group, and +4.3 ± 0.6 D in the untreated group. All three groups showed an overall reduction in hyperopia. On average, the treated hyperopes initially emmetropized more slowly than the untreated group, with a mean 1.0 D more hyperopia at 18 months, but the difference had narrowed by 36 months, with a final mean of +3.4 D in the treated group and +3.1 D in the untreated, an overall reduction of 1.2 D in both groups. The control group emmetropized by a small amount, with a mean reduction of 0.3 D. The hyperopic groups showed an increase in variability between 9 and 36 months (0.9-D increase in SD in each group).

Analysis of variance comparing treated and untreated groups found that the age–treatment interaction that marks the temporary advantage of the untreated group at 18 months was significant (F = 5.42, P < 0.03), but an independent samples t-test comparing the treated and untreated means at 36 months found no significant difference between the two groups. Power calculations indicate that these samples would have a power of 0.88 in detecting a true difference of 1.0 D in the final level of hyperopia and 0.34 in detecting a 0.5-D difference at the 0.05 significance level.

The analysis considered overall refractive outcome by taking whichever meridian was most hyperopic at each point. However, this is not necessarily a measure of developmental changes in any specific meridian or eye, because it may compare different meridians at different times. An alternative approach is to track whichever meridian is most hyperopic at 9 months for each child. This yielded an overall pattern of change very similar to that in the previous analysis, with a mean difference of 1.1 D between the treated and untreated groups at 18 months. The overall reduction of hyperopia was greater using this measure, however, with a final mean of +2.7 D for the untreated hyperopes and +3.0 D for the treated, a reduction of 1.6 D in both groups. The control group had a final mean of +1.4 D, a reduction of 0.5 D. Analysis of variance for the two hyperopic groups again found a significant age–treatment interaction (F = 9.35, P < 0.005), and an independent samples t-test found no difference at 36 months (power = 0.89 for a true difference of 1.0 D; 0.35 for 0.5 D at P < 0.05).

Of the 44 treated-group subjects in our main longitudinal analysis, 13 did not meet the criterion for compliance. We reanalyzed the data for the treated group, omitting these children. Figure 2 plots the mean level of hyperopia, calculated as the most hyperopic meridian at the time of measurement, distinguishing the treated hyperopes who were compliant from those who were not.

The mean greatest axis in the compliant treated group was +4.5 D at 9 months, compared with +4.3 D in the untreated group. The compliant treated group mean at 18 months was +3.7 D, 0.8 D higher than the untreated mean, but decreased to +3.3 D by 36 months, leaving a final difference of only 0.2 D between the two, an overall reduction of 1.2 D in both groups. Analysis of variance again found a significant age–treatment interaction (F = 6.31, P < 0.02). An independent samples t-test found no significant difference at 36 months.
Again, the data were reanalyzed in terms of the single greatest axis at 9 months. At 18 months the untreated group mean was 13.4 D, 1.1 D higher than the treated compliant group, but by 36 months the mean had declined to 12.9 D, leaving a difference of 0.2 D between the two, an overall mean reduction of 1.6 D in both groups. Analysis of variance again found that the age–treatment interaction was significant (F = 11.81, P < 0.02), but the final difference in means was not (power = 0.85 for a true difference of 1.0 D; 0.32 for 0.5 D at P < 0.05).

When we included in these four analyses the infants without a midpoint refraction (total n = 148), the results were essentially unchanged, although the control group showed slightly less reduction in hyperopia than in the analyses shown in Figures 1 and 2. An example of these analyses is shown in Figure 3 (the larger samples increase power to 0.96 for a true difference of 1.0 D, 0.45 for 0.5 D at P < 0.05).

All these analyses found a greater overall change in refraction in the hyperopic groups than in the control subjects. To study the relationship between level of hyperopia at 9 months and amount of emmetropization by 36 months, we put aside our groupings and examined the continuum across the full range of refractions. Because treatment had been shown to make no significant difference to outcome at 36 months, we considered both hyperopic groups together in the same analysis. In addition to the 148 infants for whom we have a 9-month and a 36-month measure, we also included 11 of the 18 high hyperopes who had been excluded from the trial of treatment but still participated in the study for a 36-month measure, extending the range over which we could examine the relationship.

Figure 4 plots change in hyperopia against refraction at 9 months, for the meridian initially most hyperopic in each case. The plot indicates that subjects across the whole range of initial measurements tended to converge toward emmetropia, and that a subject’s overall change was proportional to the initial degree of hyperopia. A regression analysis found this linear relationship to be highly significant (F = 56.35, P < 0.0001).

Astigmatism

Figure 5 plots the course of astigmatism, calculated as the difference between orthogonal meridians of the eye more astigmatic at 9 months, for the 117 infants for whom we had a 9-, 18- and 36-month measure. The treated group comprised all intention-to-treat subjects, both compliant and noncompliant. The mean astigmatism of all three groups reduced over time: in controls it declined from 0.8 D at 9 months to 0.3 D at 36 months; in treated hyperopes, from 1.9 to 1.0 D; and in
untreated hyperopes, from 1.7 to 0.7 D. Analysis of variance comparing the two hyperopic groups found no significant age-treatment interaction, and an independent samples t-test found no significant difference between the final means at 36 months (power >0.99 for a true difference of 1.0 D; 0.79 for 0.5 D at \( P < 0.05 \)). The same analyses comparing data from only the compliant subjects in the treated group (\( n = 31 \)) with the untreated group again found no significant interaction or final difference (power >0.99 for a true difference of 1.0 D; 0.81 for 0.5 D at \( P < 0.05 \)).

Of the 85 subjects with 1 D or more of astigmatism at 9 months, 49 were vertical (against the rule, the most hyperopic meridian between 45° and 135°) and 36 horizontal (with the rule, the most hyperopic meridian 0° to 45° or 135° to 180°). Analyzing these two types of astigmatism individually, we once again found no significant effects or interactions, and no significant difference between treated and untreated group means at 36 months. This result remains the same whether we analyze the groups according to intention-to-treat or include only compliant subjects in the treated group.

To determine whether a relationship exists between initial astigmatism and its reduction by 36 months, a regression analysis was performed (Fig. 6) for the same group of infants used in our regression analysis of emmetropization (\( n = 159 \)). In each infant, we tracked the eye that was more astigmatic at 9 months. Comparing astigmatism (expressed as a signed value obtained by subtracting the vertical meridian from the horizontal), with change (expressed as the difference between astigmatism values at 36 months and 9 months), we again found a highly significant linear relationship (\( F = 315.86, P < 0.0001 \)).

As Figure 6 indicates, there is a very strong tendency for astigmatism of either type to diminish in proportion to its original extent. The bottom left and top right quadrants, which contain subjects in whom astigmatism increased, were very sparsely populated. Our longitudinal analysis of the group means (Fig. 5) indicates that this process of reduction was not impaired by the prescribed partial correction: The protocol applied meant that in only 22 cases did this include a cylindrical correction.

Possible Biases

To evaluate differential withdrawal from the study as a possible source of bias, we compared the initial (9 month) retinoscopy measures of greatest axis and astigmatism of subjects who remained in the study with those who were withdrawn. Independent samples t-tests found no significant differences, in either hyperopic group or in the control subjects. There was also no statistically significant difference in numbers of boys and girls in any of the three groups.

DISCUSSION

Although the effects of visual feedback on emmetropization in early life are well documented, the implications of these effects for the practice of refractive correction in infancy and early childhood have not yet been well understood. This study presents the first evidence, to our knowledge, based on a controlled trial in human subjects, of whether early spectacle correction affects refractive development.

Emmetropization

Our data show that, for the group as a whole, a substantial reduction of hyperopia, both spherical and cylindrical, occurs during the second and third years of life. The average reduction of refractive error is a linear function of the initial level. The regression lines imply that a child with an initial refraction of +0.86 D would on average show zero change in this meridian, and so the process of emmetropization can be considered as a convergence of refractions toward a low hyperopic value. The linear relationship directed to a low hyperopic end point is consistent with our data in other groups of both hyperopic and myopic infants.\(^1\,\,2\,\,5\) The change in astigmatism is also proportional to initial refractive error, implying convergence toward a near emmetropic value in the case of the cylindrical as well as the spherical component of refraction, consistent with earlier data on the reduction of infant astigmatism.\(^2\,\,6\,\,27\,\,24\)

It must be appreciated, however, that there is substantial variability in the extent of emmetropization within the hyperopic group. It is apparent from Figure 4 that some infants show marked reductions in hyperopia over the first 3 years of life, whereas others show little change. The basis of this variability is not yet known.

The occurrence of withdrawal between 9 and 36 months raises the question of whether those who remained in the study were a biased sample. However, we found no evidence for any differences in initial refraction between children who were withdrawn and those who remained in the study.

Effect of Spectacle Correction

The comparison of corrected and uncorrected groups suggests a small, transient effect of refractive correction between 9 and 18
months of age. However, by 36 months this effect had disappeared, and the infants with initial hyperopia had reached a common refraction irrespective of treatment. This conclusion remained the same whether we analyzed in terms of the original assignment to treated or untreated groups, or whether we considered as treated only those who consistently wore their spectacles. Thus, we find no evidence that partial spectacle correction for infantile hyperopia interfered in any persistent way with the developmental trend toward emmetropization.

The analysis that included the largest number of hyperopes—all those with a 9 month and 36 month measurement (total n = 89)—had a power of 0.96 in detecting a true difference of 1 D at P < 0.05. Thus, although there is wide variability in initial refraction and refractive change, with groups of this size we can show with some confidence that spectacle correction does not substantially interfere with emmetropization.

The general reduction of hyperopia meant that many infants (n = 21) in the treated group did not fulfill the criteria for prescription before the age of 36 months.

The finding that spectacle correction did not impede emmetropization applied to the refractive population we have described. We cannot be sure how corrective correction might affect the development of very large hyperopic errors, which show very variable degrees of emmetropization (see the squares in Fig. 4), or how it would affect children who have strabismus before receiving a correction. We did not gather systematic data on ethnic origin or socioeconomic status. However, the study group and the population from which it is drawn had a very strong predominance (>90%) of white origin, and because the screening was based on high attendance within a socially mixed geographic area, covers the range of socioeconomic groups. There was no indication of differential withdrawal between different districts within the overall area.

Our results are also specific to the practice of partial spectacle correction as described in the Methods section. A full correction of refractive error would ensure that the accommodative demand for an infant with hyperopia was reduced to a lower level than for control infants (who in general had a small, uncorrected hyperopia). It is possible that such a reduction in accommodation would influence the emmetropization process. However, our partial corrections did not produce such an effect.

We have found that the partial refractive correction of infants with hyperopia according to the protocol described in the present study has beneficial effects of reducing the incidences of strabismus and poor acuity by two thirds in children who comply in wearing the prescribed correction. The present results indicate that these benefits can be achieved without the optical treatment’s impairing the normal developmental regulation of eye growth and refraction.

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References


