Undercorrection of myopia enhances rather than inhibits myopia progression

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Abstract

The effect of myopic defocus on myopia progression was assessed in a two-year prospective study on 94 myopes aged 9–14 years, randomly allocated to an undercorrected group or a fully corrected control group. The 47 experimental subjects were blurred by approximately $+0.75$ D (blurring VA to 6/12), while the controls were fully corrected. Undercorrection produced more rapid myopia progression and axial elongation (ANOVA, $F(1, 374) = 14.32$, $p < 0.01$). Contrary to animal studies, myopic defocus speeds up myopia development in already myopic humans. Myopia could be caused by a failure to detect the direction of defocus rather than by a mechanism exhibiting a zero-point error.
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1. Introduction

The refractive development of the eye is under the influence of a feedback mechanism known as emmetropization where optical defocus guides the growth of the eye so that there is no refractive error (Hung, Crawford & Smith, 1995; Schaeffel, Glasser & Howland, 1988; Troilo & Wallman, 1991). This requires that the visual system is able to distinguish between myopic defocus (where the optical image is formed in front of the retina) from hypermetropic defocus (where the image plane is behind the retina).

When the primate emmetropic eye is deprived of form vision by degrading the optical image, it becomes myopic (Raviola & Weisel, 1977; Wallman & McFadden, 1995) and restoring an undegraded image results in a growth of the eye towards emmetropia again. A similar response has been found in most (but not all) species examined.

Although there is general agreement that growth of the young human eye is regulated by an emmetropization mechanism, refractive errors occur in between 20% of the adult population in European populations, and up to 80% of the population in some Asian countries. The reason for this anomaly is not clear, as the retinal image is defocussed in myopes rather than degraded. Possibly the error detection system in these individuals is flawed, or the eye may be growing towards an "incorrect" zero (Medina, 1987a,b).

If the emmetropization mechanism is defective in detecting the sign of defocus, then it is possible that human myopia is an inappropriate response to a signal, which would better result in a growth response in the hypermetropic direction. If the mechanism is merely showing a zeroing error then undercorrecting myopia should slow down or halt the progression of eye growth. There is little reliable information on the effect of undercorrection in humans. Only one poorly controlled clinical trial has been carried out on myopes (Tokoro & Kabe, 1965). However where spectacles are not worn for close work there was no significant effect on myopia progression (Ong, Grice, Held, Thorn & Gwiazda, 1999).

We report here the results of a randomised controlled clinical trial to determine the effects of undercorrection on the rate of progression of myopia. Our results show that undercorrection speeds up the rate of myopia progression in myopic children, which supports the idea that their emmetropization mechanism is defective in detecting blur.

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2. Methods

2.1. Subjects

This study was a single masked randomised controlled clinical trial. One hundred and six myopic subjects were recruited into the study and 12 subjects dropped out. The remaining 94 subjects participated in this study for a period of two years. Half the children were undercorrected (left slightly myopic) and the other half were fully corrected. The study was carried out at the Department of Optometry, Faculty of Allied Health Science, National University of Malaysia.

All subjects in both undercorrected and fully corrected groups wore spectacles prescribed by the study team. In the undercorrected group, the maximum distance monocular visual acuity was maintained at 6/12 (20/40) in each eye (usually achieved by about +0.75 D addition to each eye in the full correction) throughout the study. In the fully corrected group, monocular visual acuity was maintained at 6/6 (20/20) or better in each eye.

When a subject was referred, the history, age, sex and race were taken, and an initial static retinoscopy was performed by an optometrist. If the subject satisfied the selection criteria based on age, sex, race and initial refractive error, he or she was then be given an appointment with the patient care unit. Those patients that did not satisfy the selection criteria would be cared for in the optometry teaching clinics.

The patient care unit consisted of two optometrists. They carried out the initial examination to determine the suitability of subjects. The task of the patient care unit was to prescribe glasses for each subject as well as to counsel subjects and their parents in the correct use of the glasses and to provide a follow-up examination every six months for the duration of the study. The initial examination consisted of a full optometric routine examination.

Subjects were all schoolchildren. They were accepted into the study on basis of the following selection criteria:

(1) Age 9–14 years old.
(2) Myopia with spherical equivalent refractive error of −0.50 D or more in both eyes, with no principal meridian being plano or having any amount of plus power.
(3) No more than two dioptres of astigmatism in each eye.
(4) Corrected visual acuity of 6/6 or better in each eye.
(5) No significant binocular vision problems, that included anisometropia over 2.00 D, or where refractive therapy for binocular vision problems was required. Those having strabismus and amblyopia were excluded.
(6) Normal ocular health.
(7) No previous contact lens wear.
(8) Family was not planning to move out of the area in the near future.
(9) Willingness to give written consent.

After a subject was accepted into the study, he or she was placed into either the undercorrected group or the fully corrected group (see Section 2.2).

Following the allocation of subjects, each subject was then referred to an evaluation unit that comprised only one full-time optometrist. The task of the evaluation unit was to evaluate subjects before entering the study and to re-evaluate each subject every six months for a period of two years. The following procedure was carried out as the masked database used to assess treatment:

1. Static retinoscopy (non-cycloplegic).
2. Keratometry.
3. Subjective cycloplegic refraction, using the endpoint "maximum plus or minimum minus for best acuity".
4. Ocular components measurements by means of A-scan ultrasonography.

After completion of the evaluation unit examination, each subject was returned to the patient care unit to obtain their correction. Subjects were instructed to wear their glasses all the time except during sleeping. Six-month appointments for the follow-up examination were given.

During all these examinations, the evaluation unit was not aware of the experimental group to which subjects belonged. The two study units kept separate records. The evaluation unit did not check lens prescriptions, and was not allowed to look at patient care unit records. The evaluation unit was not allowed to question subjects concerning their glasses. At each six-month follow-up, the patient care unit monitored the subjects' compliance in wearing glasses through a series of questionnaires, which were formulated similar to that of Hemminki and Parssinen (1987).

2.2. Sampling, control and case allocation

Each subject was assigned by the patient care unit to either the control group or the treatment group on a matched basis for age, sex, race and initial refractive error. Only subjects of Malay and Chinese ethnic origin were used in this study. Age was considered based on the date of birth. Three age categories were used based on the age at baseline measurements: 9–10, 11–12 and 13–14 years old. Initial refractive error was determined by subjective refraction (non-cycloplegic). The criterion for acceptance into the study was −0.50 D (spherical equivalent) or more in each eye. For refractive error, four categories were used: −0.50 D to −0.87 D; −1.00 D

to −1.87 D; −2.00 D to −2.87 D, and −3.00 D and more myopic.

For allocation of subjects, a block randomization technique described by Zelen (1974) was used, as follows:

The treatment group and the control group consisted of 48 separate cells, derived as follows:-

(two racial groups) × (two gender categories)

  × (three age categories)

  × (four refractive error categories)

  = 48 cells.

Subjects were paired by the patient care unit so that both subjects in a pair belonged to a single cell above. One subject was designated subject 1, and the other designated subject 2. One subject was to be allocated to the treatment group and the other subject allocated to the control group based on a predetermined randomization procedure. We used a coin-toss to randomise the allocation. On the toss of a coin, if heads came up then subject one was allocated to the undercorrected group and subject two was allocated to the fully corrected group. If tails came up, then subject one was allocated to the fully corrected group and subject two was allocated to the undercorrected group. This procedure was repeated for each pair of subjects.

2.3. Frame selection and dispensing

All the patients were dispensed CR-39 plastic lenses. In the fully corrected group, a subject's lens prescription would be changed when there was a change in the monocular subjective finding (using the "maximum plus or minimum minus for best acuity" endpoint) of 0.50 D more plus or more minus power (equivalent sphere) for one or both eyes, as compared to the subject's current lens prescription.

In the undercorrected group, a subject's lens prescription was always changed by adding a positive power to blur vision, and maintained to give a vision of 6/12 each eye.

2.4. Ethical considerations

Parents and subjects were informed about the programme and its potential risks and benefits, and their written consent were obtained. Should any signs of ill effects arising from treatment occur, or if any other contraindications were found, subjects would immediately be referred for appropriate treatment and if necessary they would be excluded from the study. Subjects were free to withdraw from the investigation at any time. This research was approved by the National University of Malaysia's Committee on the use of humans as experimental subjects and it followed the tenets of the Declaration of Helsinki.

2.5. Statistical analysis

Results were only analysed after the last reading of the last patient was collected. The mean and mean changes with respect to baseline data in various parameters between undercorrected and fully corrected groups were analysed by both parametric and non-parametric tests using SPSS for Windows (Ver 6.0) statistical package. The parametric tests include ANOVA and Student's t-test, while a non-parametric test includes chi-squared test.

Since the right eye and left eye are not independent, (Ray & O'Day, 1985) the average values of right and left eyes were used in all the subsequent analysis. In analysing the refractive error data, the mean spherical equivalent was used. A mean spherical equivalent was calculated as sphere power plus half the signed cylindrical power.

2.6. Compliance

Full compliance was defined as wearing glasses for at least 8 h a day. Forty subjects in the undercorrected group complied fully while 41 subjects in the fully corrected group complied fully. Partial compliance was defined by wearing glasses for at least 6–8 h. Six of the fully corrected group complied partially with the wearing schedule while seven subjects in the undercorrected group complied partially with the wearing schedule. All the subjects complied either partially or fully with the wearing schedule. There was no difference in the spectacle wearing habits of the undercorrected and fully corrected groups.

3. Results

3.1. Base-line data for subjects completing the study

At the start of the study, the characteristics of subjects in the undercorrected group and fully corrected group were very similar. There were no significant differences (Chi-squared, $p > 0.05$) in mean initial age, initial period of wearing glasses, gender, racial makeup, initial refractive error or axial length between the undercorrected group and the fully corrected group (see Table 1).

3.2. Results of two-year optical treatment

Fig. 1 shows the mean changes in refractive error for the undercorrected group and the fully corrected group over the two-year period of the study. All the changes in refractive error were derived by subtracting the baseline

Table 1
Some characteristics of subjects before the optical treament

	Undercorrected	Fully corrected	Significance
	(Mean ± SD)	(Mean ± SD)	
Initial age (years)	11.48 ± 1.48	11.64 ± 1.48	NS
Initial duration of spectacle wear (years)	0.75 ± 1.39	0.88 ± 1.04	NS
Gender			
Males	18	21	
Females	29	26	NS (Chi-squared)
Race			
Chinese	20	21	
Malay	27	26	NS (Chi-squared)
Initial refraction (D)	−2.68 ± 1.17	−2.68 ± 1.41	NS
Axial length (mm)	24.13 ± 0.57	24.19 ± 0.89	NS

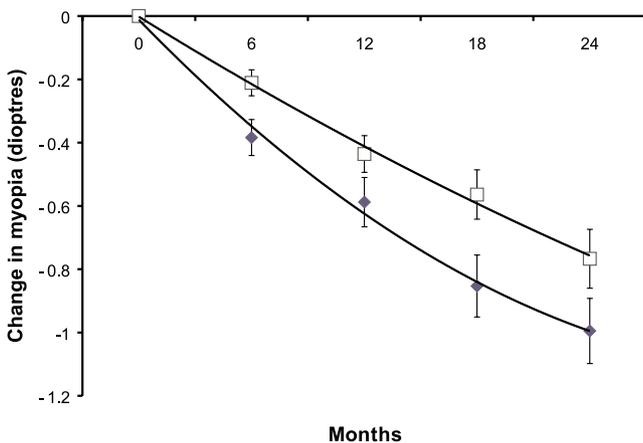Undercorrected subjects wore a reduced correction during the study. NS: Not significant.

Fig. 1. Mean changes (vertical bars show ±1 SEM) in refractive error for the undercorrected group (filled symbols) and the fully corrected group (open symbols) over the two-year period of the study. There were 47 subjects in each group. The undercorrected group showed a greater rate of progression as compared to the fully corrected group (univariate ANOVA, $F(1, 374) = 14.32$, $p = 0.001$).

Fig. 2. Mean changes (vertical bars show ±1 SEM) in axial length for the undercorrected (filled symbols) and the fully corrected group (open symbols) over the two-year period of study. There were 47 subjects in each group. The undercorrected group showed a greater axial length elongation than the fully corrected group (Univariate ANOVA, $F(1, 374) = 4.13$, $p = 0.04$).

mean values from mean values at 6-month, 12-month, 18-month and 24-month follow-up. At the end of the 24 month period, the mean progression in the undercorrected group was −1.00 D, whilst in the fully corrected group it was −0.77 D. The undercorrected group showed a significantly greater rate of progression as compared to the fully corrected group (univariate ANOVA, (2 treatment groups, 376 refractive error measurements in each group) $F(1, 374) = 14.32$, $p < 0.01$).

Fig. 2 shows the mean changes in axial length for the undercorrected group and the fully corrected group over the two-year period of the study. The undercorrected group showed a greater axial length elongation than the fully corrected group (univariate ANOVA (two treatment groups, 376 axial length measurements in each group) $F(1, 374) = 4.13$, $p = 0.04$). There were no significant differences in other ocular parameters such as corneal curvature, anterior chamber depth and lens thickness between the undercorrected group and the f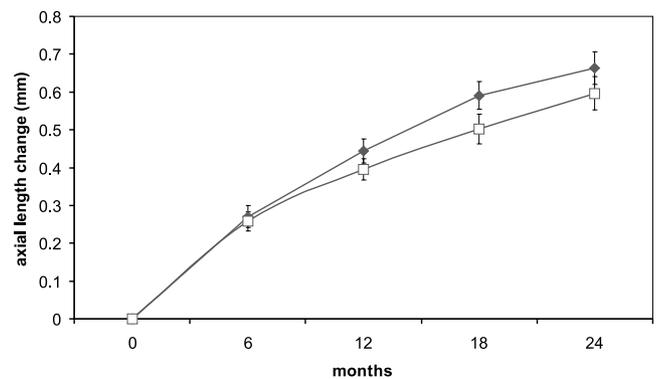ully corrected group. Nor was there any significant difference in daily reading hours after school between the undercorrected group and the fully corrected group.

4. Discussion

Our findings provide strong evidence that myopia is caused by a malfunction of the sign detection mechanism in emmetropization rather than by a zero point error, as suggested by Medina (1987a,b). The former problem means that both myopic and hypermetropic defocus may produce a myopic response in eye growth, whereas a zero point error would result in the eye's refractive error stabilising at a myopic value; myopia progression would then slow or stop when this error was approached.

Our findings do not support the conclusions of a previous undercorrected study (Tokoro & Kabe, 1965), which suggested that the mean change in refractive error is significantly reduced in the undercorrected group as compared to the full-time fully corrected group. This earlier study did not match subjects for age, and used a

very small sample size. Some subjects were also receiving other pharmaceutical treatments such as neosynephrine and tropicamide as part of another study (Tokoro & Kabe, 1964), and a detailed review by Goss (1982) concluded that the statistical treatment of the data was flawed.

Myopic children show a lower gain in accommodation responses when they develop myopia. Although they accommodate near normally to proximal targets they fail to respond appropriately to minus lenses, possibly indicating the lack of a defocus detection mechanism operating in at least one direction of defocus (Gwiazda, Thorn, Bauer & Held, 1994, 1995). Since these children were initially emmetropic, it seems that the emmetropization mechanism that was operating initially is no longer able to regulate eye growth correctly. In comparison with emmetropes, myopic young adults also show a deficient response to minus-lens induced blur when looking at a distant object (O'Leary & Allen, 2001), which is in line with the findings of Gwiazda et al. (1994, 1995).

Other aspects of the optical performance of myopic eyes are also abnormal. Many myopic eyes have more severe axial aberrations than normal, and where aberrations in myopic eyes are relatively normal for distance viewing, they may show increasing aberrations with accommodation, which is the opposite to the change in the non-myopic eye (Collins, Wildsoet & Atchison, 1995). It seems unlikely that these aberrations, which have a relatively small effect on the retinal image clarity in comparison to the effects of myopia, are the cause of the myopia. It is possible that the emmetropization mechanism is normally responsible for controlling the development of all aberrations, not only axial defocus.

Although we have shown that a general undercorrection of the myopia tends to accelerate the progression of myopia, it is significant that a full distance correction for myopia, taken in conjunction with a progressive reading addition, reduces the progression of myopia (Leung & Brown, 1999). We believe that this indicates that the presence of blurred vision at any distance may stimulate the progression of myopia regardless of the sign of defocus, in eyes which are susceptible.

5. Conclusions

Our findings support the hypothesis that myopes have an abnormal mechanism for detecting the direction of optical defocus of the retinal image. We suggest that this results in the stimulation of eye elongation when blur is present, rather than the expected inhibition of growth when the eye is myopic. We also conclude that the popular therapeutic strategy of undercorrecting the myopia in children may be not only unwarranted but even potentially harmful.

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