

Aberration Control and Vision Training as an Effective Means of Improving Accommodation in Individuals with Myopia

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PURPOSE. To test the efficacy of a novel dual treatment for improving accommodative accuracy and dynamics in young persons with myopia.

METHODS. Ninety-three young persons with myopia (mean spherical equivalent, -3.0 ± 1.8 D; age 16.8 ± 2.1 years; spherical aberration $+0.06 \pm 0.04$ μm) participated in the study. Custom-designed soft contact lenses were used to alter ocular SA to -0.10 μm to improve accommodative accuracy and reduce any lag of accommodation. A vision training regimen was performed for 18 minutes per day for up to 6 weeks to improve speed of dynamic accommodation. Control groups had contact lenses with no added SA and/or no exercises. To avoid any effects of natural levels of negative aberration on the results of the study, all participants who had negative SA were excluded.

RESULTS. The treatment contact lenses produced a significant reduction in lag of accommodation ($P < 0.05$) at all proximal viewing distances measured. The vision training measurement and treatment resulted in a significant increase in distance facility rate for all groups compared with their own baselines ($P < 0.05$). Near facility rate improved in the vision training treatment group only compared with its baseline ($P < 0.05$). Both positive and negative response times for distant viewing were significantly shorter in all groups after training compared with their baseline values ($P < 0.05$). At near, the positive response times were decreased significantly ($P < 0.05$) in both groups, whereas the negative response times decreased significantly only in the vision training treatment group.

CONCLUSIONS. After 3 months, the dual treatments (altering SA and vision training) used in the study were effective in modifying accommodation. The static accommodative response to targets at proximal distances was increased by the altered SA

contact lenses and rates of dynamic accommodation improved with vision training. (*Invest Ophthalmol Vis Sci.* 2009;50:5120-5129) DOI:10.1167/iov.08-2865

Myopia affects approximately 25% of adults in Caucasian populations¹⁻⁴ and has a greater (and possibly increasing) incidence in Asia.⁵⁻⁸ Because there has been a rapid increase in the prevalence of myopia in certain populations⁹⁻¹¹ and in certain subgroups of the population,¹² we may infer an environmental contribution to myopia's development. Animal studies show that form deprivation and lens-induced blur can induce myopia through degradation of the quality of the retinal image.¹³⁻¹⁶ Although there are limitations in the application of the animal study findings to humans,¹⁷ at present these seem to be the only proven environmental factors for consistently inducing myopia.

Persons with myopia show several anomalies of accommodation that may contribute to retinal image degradation. An increased lag of accommodation¹⁸⁻²³ may be linked to progressing myopia²³⁻²⁶ and increased accommodative variability in those with myopia^{27,28} that results in retinal defocus during near work. This retinal defocus could be integrated over time²⁹ to provide a myopigenic stimulus.

The increase lag of accommodation in myopia is accompanied by a shallower accommodation stimulus response function. It is found in response to targets at various distances in real space^{20,21,24} and also with negative defocusing lenses and a fixed distance target.²⁰

Reduced accommodative facility is associated with both myopia³⁰⁻³² and its progression.²⁴ Accommodative response times to step stimuli are longer in myopia.^{28,33,34} Increased lag of accommodation and reduced accommodative facility are independently associated with myopia's progression in young adults.²⁴

We have previously suggested that optical aberrations may be a cause of some of these accommodative anomalies.^{35,36} Although some have found myopic eyes to have elevated higher order aberrations when compared to emmetropic eyes,³⁷⁻³⁹ others have found no correlation between refractive error group and spherical aberration⁴⁰ or between refractive error magnitude and total root mean square higher order error or spherical aberrations.^{41,42}

Radhakrishnan et al.³⁵ showed that negative lenses produce a markedly smaller reduction in distance visual acuity in corrected myopia than in emmetropia, but positive lenses produce the same reduction in visual acuity in the two groups. Similarly, myopic eyes show a greater asymmetry in the loss of contrast sensitivity with positive versus negative lenses than is found in emmetropic eyes, particularly at intermediate spatial frequencies.³⁶ These differences were similar to those that would be expected in the presence of greater amounts of fourth-order SA in myopic eyes.

Several studies have examined the changes in both SA and other higher order aberrations with accommodation⁴³⁻⁴⁹ with

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TABLE 1. The Four Treatment Groups in The Cambridge Anti-myopia Study

Altered spherical aberration and vision training
Vision training only
Altered spherical aberration only
No change to spherical aberration and no vision training

somewhat equivocal results. He et al.,⁴⁷ Ninomiya et al.,⁴⁸ and Cheng et al.⁴⁹ found that SA changes in a negative direction with accommodation, whereas Atchison et al.⁴⁵ found this change in only half of their subjects. Several groups observed considerable changes in coma but these varied in direction and magnitude.^{43-45,47,49} Few studies have addressed the relationship between aberrations, accommodation, and refractive error, and their findings have been inconsistent. He et al. (*IOVS* 2003;44:ARVO E-Abstract 2122) found that in a group of young adults, ocular aberrations decreased with accommodation in emmetropic eyes, but in myopic eyes, aberrations increased or did not change. This suggests that, at near, those with myopia have greater amounts of higher order aberrations than emmetropic persons. However, Hazel et al.⁵⁰ found that individuals with emmetropia and myopia both demonstrated an increase in negative SA with accommodation, whereas Collins et al.⁵¹ found that the mean squared fourth-order aberrations of a myopic group were lower than those of an emmetropic group when accommodating by 0, 1.5, and 3 D.

Higher-order optical aberrations may affect the accommodative response by causing a degradation of the retinal image (which extends the depth of field of the eye), or by altering the sensitivity to negative defocus.⁵² The theoretical relationship between SA and modulation transfer at optimal focus⁵³ predicts a more myopic optimal focus with the introduction of positive SA, especially at lower spatial frequencies. Moreover, even-order aberrations (similar to spherical aberration) could provide cues for accommodation.⁵⁴

Several studies have attempted to arrest myopia progression in children using multifocal spectacle lenses.⁵⁵⁻⁶² Both bifocal^{55,56} and progressive addition lens (PAL) studies⁵⁷⁻⁶² have met with limited success. The COMET study⁵⁹ showed that multifocal lenses were effective in slowing myopia progression during the first year but not thereafter. However, in these longitudinal studies, the effect of the near addition lenses on accommodation was not monitored during the trials.

It has been assumed that multifocal lenses reduce the lag of accommodation based on work with single vision lenses⁶³; however, there is evidence that a near addition can produce a lead of accommodation in both spectacles⁶⁴⁻⁶⁷ and bifocal soft contact lenses,⁶⁸ resulting in myopic retinal defocus. Jiang et al.⁶⁹ sought to establish the near addition that would optimize accommodative accuracy and found that much lower powers of near addition than those used in bifocal lens and PAL clinical trials were needed.

On the assumption that accommodative lag is a cause of myopia's progression, there seem to be several possible explanations why the COMET trial was not entirely successful in halting it: (1) Subjects wearing progressive addition lenses may have adapted to the lenses after some weeks or months of wear and redeveloped a lag of accommodation; (2) extrafoveal image quality may have been degraded due to the design of progressive addition lenses; for example, derived from higher order^{70,71} and/or off axis⁷² aberrations; (3) the lenses may have left the participants myopic at near. The detrimental effects of both hypermetropic and myopic retinal defocus are supported by the increase in myopia caused by overcorrection⁷³ and undercorrection.⁷⁴

Accommodation can be improved through vision training⁷⁵⁻⁸⁰ Although accommodation dysfunction has been high-

lighted as a potential causative factor for myopia progression, we could find no studies using a robust placebo-controlled design that assessed the effectiveness of vision training on myopia retardation.

The Cambridge Anti-myopia Study (CAMS) is designed to test the efficacy of a novel treatment for improving accommodative accuracy and dynamics in young persons with myopia. The treatment includes vision training and altering ocular spherical aberration.

We have recently demonstrated that when contact lenses are used to manipulate SA for periods of up to 1 hour, lag of accommodation (measured in the contralateral eye when the eye wearing the spherical aberration-altering contact lens fixated the target) increases when positive SA is introduced, and decreases when negative SA (up to 0.2 μm at 5 mm) is introduced.⁸¹

The effect of this treatment on myopia progression rates was assessed in a longitudinal clinical trial. This article shows the efficacy of the approach in a myopic population in improving accommodative responses and dynamics over an extended treatment period.

MATERIALS AND METHODS

Study Design

The treatment modality for The Cambridge Anti-myopia Study involves custom-designed contact lenses that control SA in an attempt to optimize static accommodation responses during near work, and a vision training program to improve accommodation dynamics. A factorial trial design was used to test the efficacy of the two independent treatments simultaneously. There were four possible treatment groups, as shown in Table 1.

Participants

Participants were recruited over an 8-month period and were in the age range of 14 to 22 years. Inclusion criteria for The Cambridge Anti-myopia Study are shown in Table 2. Two hundred twenty volunteers attended a baseline assessment visit, and 182 were suitable for enrollment in the study. The remainder were excluded because of unsuitable refractive error, amblyopia, corneal disease, or unwillingness to proceed. A further five participants were unable to proceed because of inability to handle the contact lenses. The randomization process was explained to all participants (and their caregivers if applicable) and agreement was reached that the participant would accept any of the treatment modalities and that they would not know to which group they were assigned during the course of the trial. Data presented here are for 93 participants with positive spherical aberration, who attended a baseline assessment visit and a follow-up of the effectiveness of the treatment on accommodation function after three months. All participants who had negative SA were excluded for the purposes of this study. The mean age of the participants was 16.8 \pm 2.1 years and the mean spherical equivalent of the refractive error for the right eye of the participants was -3.0 ± 1.8 D (-0.40 to -9.12).

TABLE 2. Inclusion Criteria for Enrollment into The Cambridge Anti-myopia Study

Age at enrollment: 14-22 years
Spherical equivalent refractive error: -0.75 to -10.00 D
Astigmatism: ≤ 0.75 D
Zero or positive levels of spherical aberration
Corrected logMAR visual acuity: 0.00 or better in each eye
No heterotropia or uncompensated heterophoria
Free of ocular disease
Free of systemic disease which may affect myopia progression
Able and willing to wear soft contact lenses for the duration of the trial

TABLE 3. Characteristics of the Participants in Each Group

Blocking Variable	CL Treatment	CL Control	VT Treatment	VT Control
Age, y	16.79 ± 2.16	16.95 ± 2.36	16.96 ± 2.11	16.81 ± 2.15
Sex, % female	54	52	59	58
Spherical myopia, D	-2.69 ± 1.74	-2.98 ± 1.92	-2.55 ± 1.87	-2.83 ± 1.71
Cylindrical myopia, D	-0.45 ± 0.30	-0.44 ± 0.28	-0.43 ± 0.27	-0.45 ± 0.29

CL, contact lens; VT, vision training.

Participants gave informed consent for taking part in the study, which adhered to tenets of the Declaration of Helsinki and was approved by the Anglia Ruskin University Ethics Committee.

Persons with anisometropia were not excluded, providing that they had good visual acuity in both eyes and good binocularity (no strabismus or decompensated heterophoria). Four subjects had anisometropia between 1.00 and 2.00 D.

To avoid any effects of natural levels of negative SA on the results of this study, all participants who had negative SA were excluded. The baseline levels of SA ranged from +0.004 to +0.225 μm . Characteristics of the participants in each group are shown in Table 3.

Randomization Procedure

Blocking variables were age, sex, and cylindrical refractive error and were stratified for spherical refractive error as shown in Table 4. One experimenter, who was unmasked, allocated participants to groups. This experimenter did not participate in any of the masked measurements and was available to look at treatment regimens with vision training and clinical issues relating to contact lens aftercare. The masked experimenters had no information about the allocation of individual participants to treatment groups.

When a participant was the first member of a block, they were randomly allocated to one of the two contact lens treatment groups by the unmasked examiner. The next member of that block was given the alternative contact lens treatment. The first matched pair in a block was allocated to the vision training control group and the second matched pair to the vision training treatment group.

Treatment Design

Altered Spherical Aberration. Soft contact lenses were designed to alter ocular SA in addition to correcting the spherical equivalent axial refractive error. The front surface curvature was calculated using paraxial optics to correct the axial refractive error. The SA of the lens was manipulated by altering the *eccentricity* of the front surface of the lens. The contact lenses were designed to alter the existing fourth-order SA of the patient to $-0.1 \mu\text{m}$ (referenced to a 5-mm-diameter pupil) while maintaining the appropriate paraxial correction. Theagarayan et al.⁸¹ demonstrated that altered SA can influence the slope of the accommodation response curve. This study showed that added positive SA significantly depresses the accommodative response slope, whereas negative spherical aberration, at least up to $-0.2 \mu\text{m}$, enhances it. The optimum improvement in the accommodative response slope was found to be with (eye+contact lens) SA levels of $-0.1 \mu\text{m}$ in an unaccommodated state. The SA of the control group lenses was designed to have 0 SA in the contact lenses, regardless of the measured

SA level of the eye. SA of $-0.1 \mu\text{m}$ for a 5-mm pupil diameter equates to 0.137 D/mm² and therefore approximately 0.34 D at the edge of a 4-mm pupil. In equivalent dioptric terms the spherical defocus required to produce the same wavefront variance as $-0.1\text{-}\mu\text{m}$ SA equates to -0.17 D.

A ray tracing program was used to calculate the required surface parameters of the contact lenses. These individually customized contact lenses were manufactured by UltraVision CLPL (Leighton Buzzard, UK) specifically for this study. All lenses were made of 58% HEMA-based material. The contact lenses were fitted such that the movement on blinking was approximately 0.25 mm. Because this small movement of the lens during blinking is likely to induce transient comalike aberration, the aberrations with these contact lenses were measured only after the lens settled in the centered position. The aberrations in the contact lenses were assessed by measuring the total aberrations of the eye after fitting the contact lens to the patient. Both the treatment and control group contact lenses were worn at least 10 hours per day.

Vision Training. The vision training regimen consisted of lens flipper exercises⁸² using a +2.00 D/-2.00 D flipper at 40 cm. The exercises were performed for 18 minutes per day for up to 6 weeks. There was a wide range of baseline accommodative facility values hence a goal-oriented approach was used. Participants were to continue with the vision training until a minimum value of 25 cycles per minute was achieved; this level is consistent with established norms for dynamic accommodation responses.^{82,83} Participants were given verbal and written instructions for the vision training and were asked to keep a log of training sessions and achievement. The training was conducted at home with the log books randomly checked for training compliance by an unmasked examiner.

Procedures

Aberration Measurement. The monochromatic wavefront aberration function of the eyes was measured using the Complete Ophthalmic Analysis System (COAS)^{84,85} with the participants viewing a distant target. Aberration measurements obtained from three consecutive readings over a pupil diameter of 5 mm were averaged in the format recommended by the Optical Society of America.⁸⁶

Accommodation Function Assessment. Accommodative response amplitudes were measured with an open field, infrared autorefractor (SRW 5000; Shin-Nippon, Tokyo, Japan).^{87,88} Measurements were obtained from the left eye, which was effectively occluded with an infrared transmitting filter (Wratten 88A; Eastman Kodak, Rochester, NY) while the right eye viewed the targets with the subjective refraction in place. Participants were instructed to keep the letters clear at all times and to inform the examiner if this was not possible.⁸⁹

For each accommodative demand, a series of five readings was taken from the left eye, and the average calculated. The accommodative stimulus values were adjusted to take account of ocular accommodative demand as the participants' refractive errors were corrected with trial lenses. Accommodation response amplitudes were calculated as the measured spherical equivalent refraction for each stimulus value minus the spherical equivalent refraction for 6.0 m. Any objective measurement of refraction may differ from the true refraction for several well-understood reasons. Our approach was intended to reduce

TABLE 4. Block Randomization Groups

Blocking Variable	Grouping Parameters
Age	14.0-17.9 years <i>or</i> 18-22 years
Sex	Male <i>or</i> Female
Spherical refractive error	0-2.00 D <i>or</i> 2.12-4.00 D <i>or</i> 4.12 to 6.00 D <i>or</i> 6.12 to 10.00D
Cylindrical refractive error	≤0.25 DC <i>or</i> >0.37 DC

0-point errors, by making the 6-m value the reference value for each participant.

Monocular Accommodative Response Amplitude to Targets in Real Space. Targets were presented in real space at distances of 6, 0.40, 0.33, and 0.25 m. For 6 m, the target consisted of a row of 20/25 Snellen letters. For the remaining distances, the target consisted of a block of words of N5 size type. The targets were presented in order of decreasing distance.

Monocular Accommodative Facility. The accommodative facility was measured at 6 and 0.4 m, for the right eye only, with semiautomated lens flippers interfaced with a computer. The software incorporated a 60-second timer and recorded the time between the flips. Participants who were unable to clear the target during the 60-second testing time had a facility rate of 0 recorded. The positive response time in this situation was recorded as 60,000 ms, although the true positive response time may have been longer. No negative response time was recorded for these participants. During the measurement of distance and near accommodative facility, the negative lens was presented first.

Accommodative facility at 6 m was measured using a plano/−2.00-D lens combination with the participant viewing 20/25 letters, whereas at 0.4 m, an N6 target was viewed through a flipper consisting of +2.00 D/−2.00-D lens combination. The effect of the negative lens on the target was demonstrated to the participants, but no other training was given before measurement. Distance accommodative facility was measured before near facility.

Statistical Design and Methods

A 2 × 2 factorial clinical trial design was used to simultaneously test the efficacy of the two treatment factors: contact lens to alter SA (absent/present) and vision training (absent/present). Each participant was assigned to one of the resulting four combinations. In addition, in each participant, measurements were taken repeatedly over two visits: baseline and 3 months. In this way, comparisons between combinations of contact lens and vision training could be made relative to between-participant variation, whereas comparisons involving visits would be made using the smaller within-participant variation. Finally, for the lag of accommodation measurement there was an additional between-participant factor: stimulus introduced at three levels.

A repeated measures analysis of variance (ANOVA) was used to take into account both the between-participant effects of the treatment factors (contact lens, vision training, and stimulus) and for the lag of accommodation the within-participant effects involving the repeated visits. In addition, Fisher's least significant difference (LSD) post hoc comparisons were made to follow up interesting or statistically significant effects due to any of the above factors alone or as part of a synergistic or antagonistic interaction with another factor (Statistica ver. 7.1; StatSoft, Inc., Tulsa, OK).

RESULTS

SA with Contact Lenses

The repeated-measures ANOVA for SA identified statistically significant differences due to contact lens treatment compared with the control ($P < 0.001$), visits ($P < 0.001$), and the interaction between these two factors ($P < 0.001$). The post hoc comparisons provided strong evidence of a significant reduction in SA due to the 3-month contact lens treatment group compared with its own baseline ($P < 0.001$) and the control group baseline ($P < 0.001$), although there was no significant change in SA in the contact lens control group between the two visits ($P = 0.396$). There were no significant effects involving vision training. The significant effects due to contact lens and visit are displayed in Figure 1.

Higher order RMS aberrations were also measured at baseline (eye only) and at the 3-month visit (eye and contact lens). There were no significant differences in higher order RMS

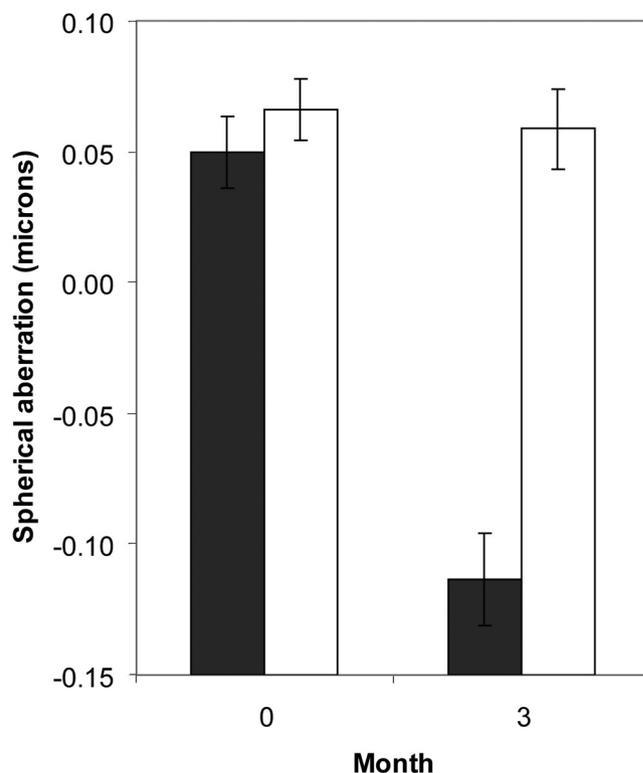


FIGURE 1. Change in spherical aberration for the contact lens treatment (■) and control (□) groups between the baseline and 3-month visits. The SA measurements were taken without contact lenses at the baseline visit (0 months) and with the contact lenses being worn at the 3-month visit. Error bars, 0.95 CI.

error between contact lens treatment and control groups at baseline (treatment, 0.19 ± 0.06 ; control, 0.20 ± 0.06 , $P > 0.05$) and at the 3-month visit (treatment, 0.28 ± 0.10 ; control, 0.26 ± 0.11 , $P > 0.05$).

Accommodative Response Accuracy

Accommodative Lag to Targets in Real Space. The repeated-measures ANOVA for lags of accommodation included effects due to stimulus in addition to contact lens, vision training and visit. There was a statistically significant interaction between contact lens treatment group and visit ($P = 0.001$). The post hoc tests provided evidence of a statistically significant increase in lag of accommodation for the contact lens control group from the baseline visit to the 3-month visit ($P = 0.029$), whereas there was a very significant reduction in lag of accommodation in the treatment group ($P = 0.001$). There was as expected no significant difference in lag of accommodation between the contact lens treatment and control groups at the baseline visit ($P = 0.215$). The significant differences can be seen in Figure 2.

There were no significant effects involving stimulus distance, nor were there any interactions between contact lens and vision-training groups. No statistically significant effect due to stimulus meant that the effects of contact lens and visit on lag of accommodation were statistically consistent across the three stimuli.

With the stimulus at 33 cm, the post hoc tests provided the greatest statistically significant reduction in lag of accommodation in the contact lens treatment group ($P = 0.002$) and significant increase in lag of accommodation in the contact lens control group from the baseline visit to the 3-month visit ($P = 0.046$). There were, however, no significant changes in lag of

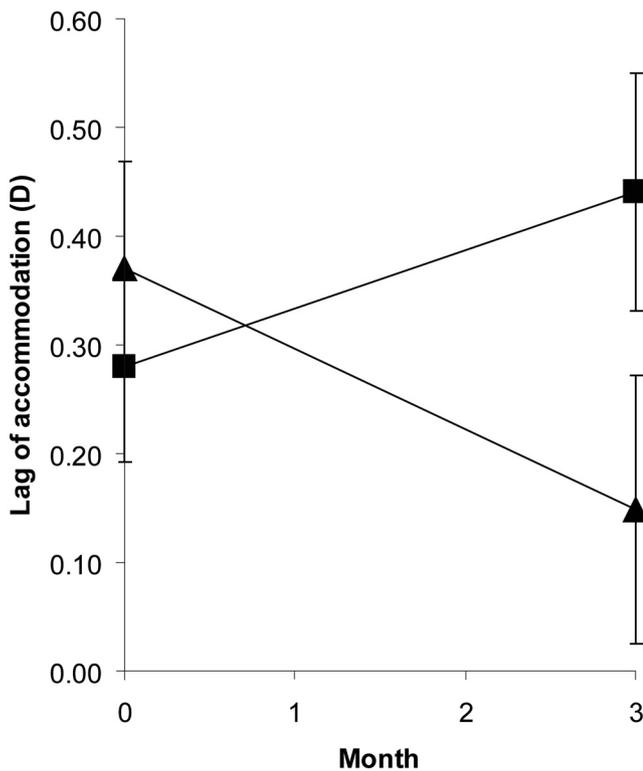


FIGURE 2. Change in lag of accommodation for the contact lens treatment (▲) and contact lens control (■) groups between the baseline and 3-month visits. Error bars, 0.95 CI.

accommodation in either the vision training treatment and control groups between baseline and 3-month visits ($P = 0.888$ and $P = 0.338$, respectively).

Accommodative Response Amplitudes to Targets in Real Space. The repeated-measures ANOVA for accommodative stimulus response function (ASRF) established a statistically significant contact lens and visit interaction ($P = 0.020$) and no statistically significant vision training effects ($P > 0.05$).

As the graphs in Figure 3 show, the interactions were due to the inconsistent differences between the contact lens treatment and control groups over the two visits. The mean ASRF slope increased for the contact lens treatment group from baseline to 3-month visits, whereas the gradient actually declined for the contact lens control group.

Post hoc comparisons identified that there were no statistically significant differences between the treatment and control groups from the baseline to the 3-month visit.

Accommodative Facility

Accommodative Facility Rates. The repeated-measures ANOVA for accommodative facility rates for both distance and near facility established that there were statistically significant differences with vision training ($P = 0.002$ for distance facility rate) and visits ($P < 0.001$ for distance and $P = 0.002$ for near facility rates) and a vision training-by-visit interaction for near facility rates ($P = 0.049$). There were no significant effects in distance and near facility rates involving the contact lens treatment factor ($P > 0.05$).

The post hoc comparisons provided strong evidence of a significant increase in:

- distance facility rate for both the 3-month vision training treatment and control groups compared with their own baselines ($P < 0.001$). There was no significant difference in dis-

tance facility rate between the vision training treatment and control groups at the baseline visit ($P = 0.158$); and

- near facility rate for the 3-month vision training treatment group compared with the baseline ($P < 0.001$) and with the control group baseline visit ($P = 0.004$). There was no significant change in near facility rate between the control group at the 3-month visit and its baseline ($P = 0.326$) and between the treatment and control group at the baseline visit ($P = 0.844$).

The significant effects due to vision training and visit for distance and near facility rates, respectively, are displayed in Figure 4.

Accommodative Response Times. To satisfy the assumptions for performing repeated-measures ANOVAs for accommodative response times, we performed a log transformation of the positive response time (PRT) data and a stronger inverse transform for the negative response time (NRT) data by using the Box-Cox procedure.

Positive Response Time. The PRT for both distance facility and near facility showed significant differences between visits ($P < 0.001$), and a significant vision training and visit interaction ($P = 0.045$ and $P = 0.048$, respectively) was observed. There were no significant effects on distance or near facility

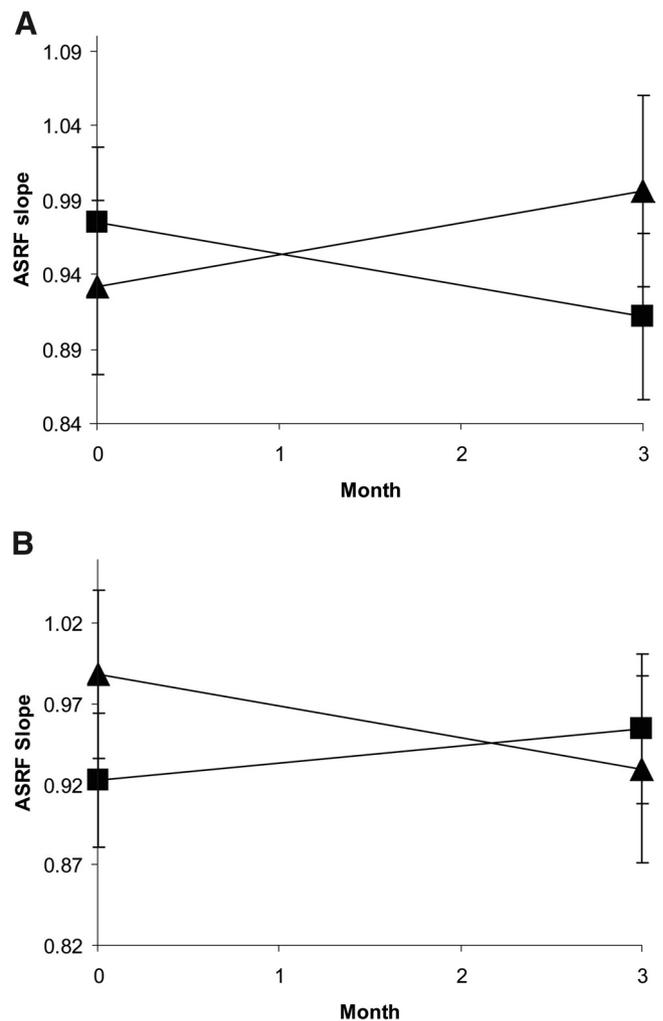


FIGURE 3. (A) Change in accommodative stimulus-response function slope for the contact lens treatment (▲) and contact lens control (■) groups between the baseline and 3-month visits. Error bars, 0.95 CI. (B) Change in accommodative stimulus-response function slope for the vision training treatment (▲) and vision training control (■) groups between the baseline and 3-month visits. Error bars, 0.95 CI.

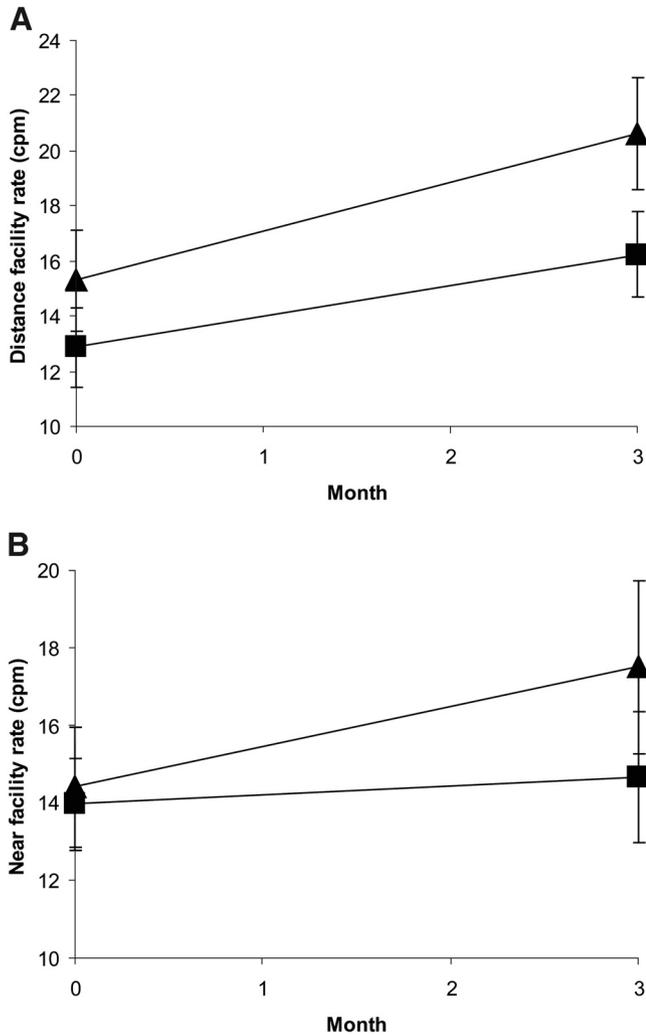


FIGURE 4. (A) Change in distance accommodative facility rate (cycles per minute) for the vision training treatment (▲) and vision training control (■) groups between the baseline and 3-month visits. Error bars, 0.95 CI. (B) Change in near accommodative facility rate (cycles per minute) for the vision training treatment (▲) and vision training control (■) groups between the baseline and 3-month visits. Error bars, 0.95 CI.

positive response times due to the contact lens treatment factor.

All pair-wise post hoc comparisons for the significant vision training and visit group combinations provided strong evidence of a significant reduction in both distance and near PRTs for the 3-month vision training treatment group compared with its own baseline visit ($P < 0.001$). There was a similarly significant reduction in the control group for both distance and near PRTs between the 3-month and baseline visit ($P < 0.001$ and $P = 0.020$, respectively). There was no significant change for either distance or near PRTs between the vision training treatment and control groups at the baseline visit ($P = 0.302$ and $P = 0.894$, respectively).

The significant effects due to vision training and visit for distance and near PRT are displayed in Figure 5.

Negative Response Time. As with PRT, there were significant effects on both distance facility and near facility NRT due only to vision training and visits. Significant differences in distance facility NRT due to vision training ($P = 0.006$) and between visits ($P < 0.001$) were observed, whereas significant differences in near facility NRT between visits ($P = 0.025$) and

a significant vision training and visit interaction ($P = 0.003$) were observed. There were no significant effects on distance or near facility negative response times due to the contact lens treatment factor.

Keeping in mind that an inverse transform was applied to the NRT data, the LSD post hoc tests provided strong evidence of a significant increase in the rate of reduction in distance facility NRT when the vision training treatment and control groups were compared from baseline visit to the 3-month visit ($P = 0.002$ and $P = 0.050$, respectively). The differences in means for near facility NRT were weaker, and only a significant increase in the rate of reduction in near facility NRT for the vision training treatment group from baseline visit to the 3-month visit was observed ($P < 0.001$). There were no statistically significant differences between the vision training treatment and control groups for both distance facility and near facility NRT at the baseline visit ($P = 0.073$ and 0.377 , respectively).

The significant effects due to vision training and visit for distance and near NRT are displayed in Figure 6.

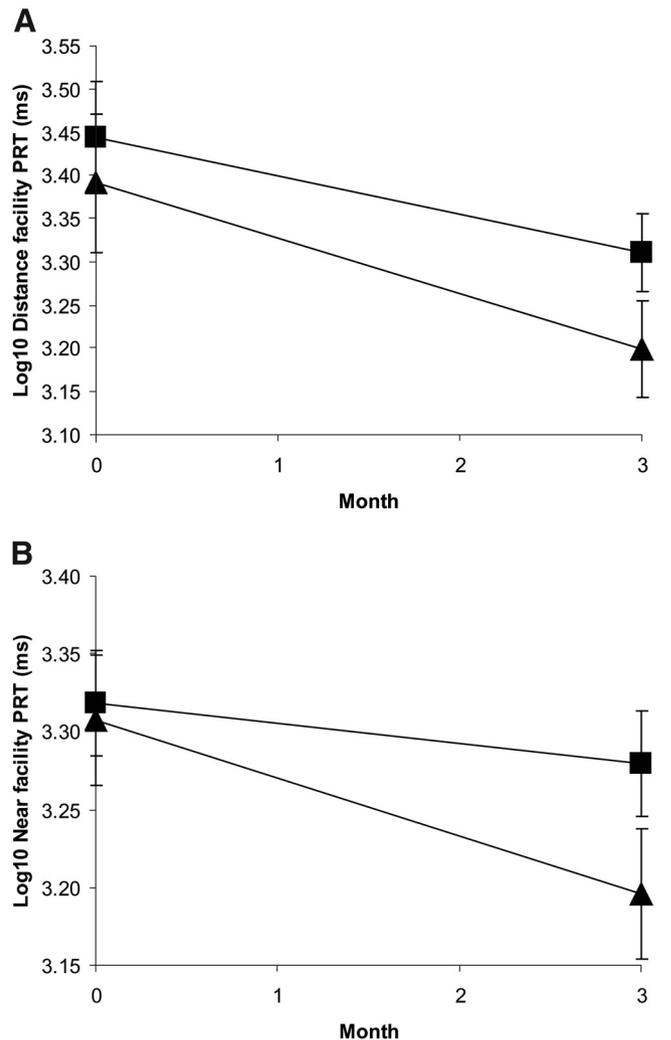


FIGURE 5. (A) Change in distance positive response time for the vision training treatment (▲) and vision training control (■) groups between the baseline and 3-month visits. Error bars, 0.95 CI. (B) Change in near positive response time for the vision training treatment (▲) and vision training control (■) groups between the baseline and 3-month visits. Error bars, 0.95 CI.

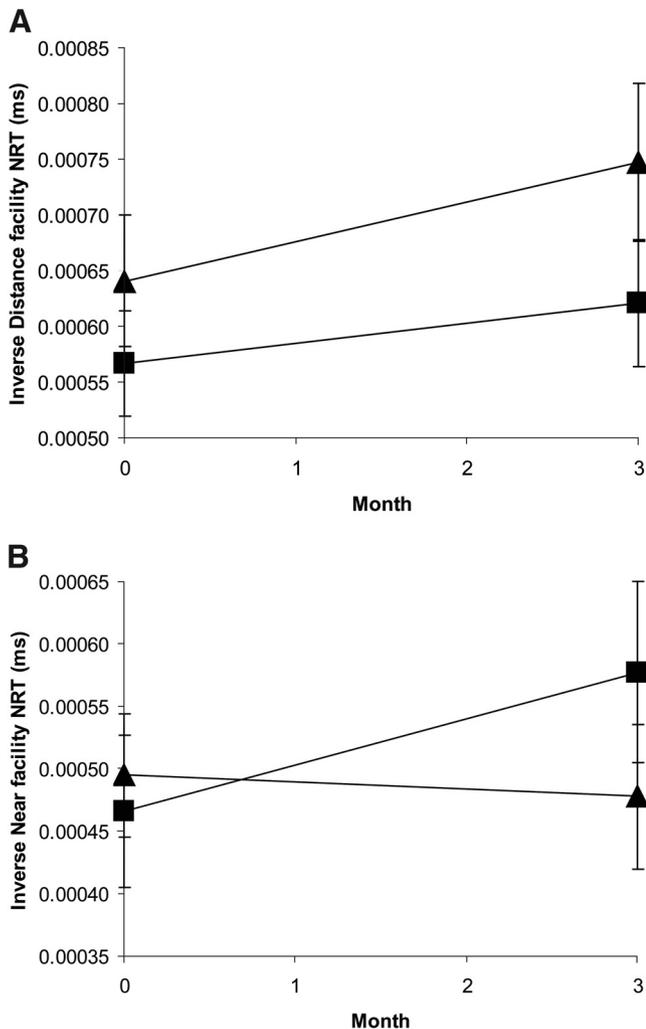


FIGURE 6. (A) Change in distance negative response time for the vision training treatment (\blacktriangle) and vision training control (\blacksquare) groups between the baseline and 3-month visits. Error bars, 0.95 CI. (B) Change in near negative response time (ms) for the vision training treatment (\blacktriangle) and vision training control (\blacksquare) groups between the baseline and 3-month visits. Error bars, 0.95 CI.

DISCUSSION

In our study, the spherical aberrations of the eye were effectively corrected or predictably altered with a custom-designed contact lens. Wearing their lenses, the treatment group had a mean fourth-order SA of $-0.113 \mu\text{m}$ and the control group a mean SA of $+0.024 \mu\text{m}$. The level of SA with the contact lens correction between the treatment and control groups was significantly different, enabling us to assess the effect of altering SA on static accommodation. The SA correction was designed to make the unaccommodated SA approximately $-0.1 \mu\text{m}$. SA is known to become more negative with accommodation in young adults.⁴⁷⁻⁴⁹ In individuals aged between 17 and 20 years, SA changes by -0.05 D/mm^2 for every diopter of accommodation.⁹⁰ The participants in the present study would therefore experience higher levels of negative SA at near in comparison to the distance aberration values.

Previous studies have assessed the effect of ocular aberrations on accommodation and on the eyes ability to determine the direction of defocus. Fernandez and Artal⁹¹ found that correcting ocular aberrations using adaptive optics resulted in a slower accommodative response, which suggests that aber-

rations play a role in accommodation. However, Chen et al.⁹² found that correcting ocular aberrations had no effect on the accommodative response gain and concluded that aberrations are not helpful in this respect. These studies enrolled a small number of subjects, making it difficult to draw definitive conclusions. A theoretical analysis by Lopez-Gil et al.⁹³ showed that odd-order aberrations were unlikely to assist in the discrimination of hyperopic defocus from myopic defocus, and this prediction was confirmed experimentally when the introduction of third-order coma and trefoil aberrations had no effect on accommodative response, except when the induced aberrations were unnaturally large. Although Wilson et al.⁵⁴ did not examine the effects of aberrations on the accommodative response, they did show that the presence of aberrations helped subjects to detect the direction of defocus, and found that even-order aberrations were especially useful in this respect. Therefore, SA could contribute toward improving both the accuracy and speed of the accommodative response. In the present study, however, the accommodative response became more accurate for proximal targets in the contact lens treatment group with no apparent change in the accommodative facility.

The higher order RMS increased in both groups after the introduction of the contact lenses; however, the levels were similar in the two groups (the contact lenses were fitted to minimize decentration in primary gaze and lens movement on blink). This result also allows us to see whether SA plays a separate role from total RMS aberration in determining accommodative response.

The aberration correction of $-0.113 \mu\text{m}$ in the treatment group increased the accommodation stimulus response function gradients and decreased lags of accommodation with the participants viewing targets in real space. This finding is in accordance with that in an earlier pilot study.⁸¹ If lag of accommodation is a stimulus for eye growth, then the treatment contact lenses used in CAMS are effective in reducing this stimulus (although not eliminating it) when the participants are viewing at close distances and may consequently slow eye growth. An unexpected finding was the deleterious effect of the control (0 aberration) contact lenses on the ASRF gradient and lag of accommodation. We are unsure of why this occurred but hypothesize that in some way the contact lenses caused some reduction in image quality resulting from residual astigmatism or surface degradation of the contact lenses. Although these changes should also be the same in the experimental group as in the control group, the improvements in the ASRF demonstrate that the SA difference in the experimental group more than compensates for any losses due to other factors. This observation is supported by the finding that high and low contrast visual acuity through the contact lenses is slightly better in the experimental group than in the control group.⁹⁴ We cannot rule out the possibility that the slight differences in visual acuity may have had knock-on effects on surface degradation by affecting blinking patterns, and thus also may have contributed to the differences in ASRF between the groups.

The purpose of the vision training program in The Cambridge Anti-myopia Study was to increase accommodative facility rates. The subjective method of measurement used has recently been shown to correlate well with a simultaneous objective accommodative facility measurement.⁹⁵ The positive accommodative response times for distance facility have been shown to be significantly longer in myopia than in emmetropia.³¹ The present study confirms that the treatment for accommodative facility is effective. Both distance and near facility rates in the vision training treatment group improved significantly from the baseline values and significantly more than in the control group. Both the positive response times and the negative response times for distance and near accomo-

ductive facility were significantly shortened at 3 months when compared with the baseline visit. The improvements were significantly greater in the vision-training treatment group than in the control group. It is interesting to note that the small amount of vision training that occurred as a result of data collection in the vision training control group was sufficient to cause an increase in accommodative facility rates as a result of a decrease in both positive and negative response times. The vision training was therefore successful in altering the particular aspects of accommodative facility that have been found to be abnormal in myopia.^{24,31,32}

Previous work in our laboratory showed that accommodative facility and the lag of accommodation when viewing near targets were significantly and independently related to myopia progression.²⁴ The Cambridge Anti-myopia Study is attempting to produce quantifiable improvements in apparently myopic accommodative functions and will assess the impact of these improvements on myopia progression. The approach used is to improve static accommodation accuracy through altered SA achieved with soft contact lenses and to improve accommodation dynamics through vision training.

The designs of other studies⁵⁵⁻⁶² that have attempted to manipulate accommodative responses to control myopia progression have not monitored changes in accommodation function during the treatment period. In the Cambridge Anti-myopia Study we will directly measure the changes in accommodative function resulting from the treatments and relate them to any change in refractive error and axial elongation. If the treatment effect regresses and/or adaptation occur, we will be able to correlate the changes in accommodation function to any alteration in the rate of refractive error change. A strength of the present study is the placebo used; as all participants wear soft contact lenses, visible differences between the treatment modalities have been eliminated. All the soft contact lenses used were specifically designed for each individual and the treatment and control contact lenses and packaging were identical in every respect apart from the levels of SA which could not be identified from the packaging.

This article has confirmed that at the 3-month point the dual treatments (altering SA and vision training) used in The Cambridge Anti-myopia Study were effective in modifying accommodation. The static accommodative response to targets at real distances was increased by the altered SA contact lenses and rates of accommodative facility improved with vision training.

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