The Cambridge Anti-Myopia Study: Variables associated with myopia progression.

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Abstract

Purpose: To identify variables associated with myopia progression and to identify any interaction between accommodative function, myopia progression, age and treatment effect in the Cambridge Anti Myopia Study.

Methods: Contact lenses were used to improve static accommodation by altering ocular spherical aberration and vision training was performed to improve dynamic accommodation. 142 subjects, aged 14-21 years, were recruited who had a minimum of -0.75D of myopia. Subjects were assigned to contact lens treatment only, vision training only, contact lens treatment and vision training, or control group. Spherical aberration, lag of accommodation, accommodative convergence /accommodation (AC/A) ratio, accommodative facility, ocular biometry and refractive error were measured at regular intervals throughout the two year trial.

Results: Ninety five subjects completed the 24 months trial period. There was no significant difference in myopia progression between the four treatment groups at 24 months. Age, lag of accommodation and AC/A ratio were significantly associated with myopia progression. There was a significant treatment effect at 12 months in the contact lens treatment group in younger subjects, based on a median split, aged under 16.9 years (p=0.005). This treatment effect was not maintained over the second year of the trial. Younger subjects experienced a greater reduction in lag of accommodation with the treatment contact lens at 3 months (p=0.03), compared to older contact lens treatment and control groups. There was no interaction between AC/A ratio and contact lens treatment effect.

Conclusions: Age, lag of accommodation and AC/A ratio were significantly associated with myopia progression. Although there was no significant treatment effect at 24 months, an interaction between age and contact lens treatment suggests younger subjects may be more amenable, at least in the short term, to alteration of the visual system using optical treatments.

Myopia is common in Caucasian and Asian populations, and its prevalence in some populations is on the increase.[1-8] In UK based populations, myopia prevalence amongst children ranges from 2.8% to 29.4% dependent upon age and ethnicity. [9-11] Both environmental and genetic factors are likely to be involved in myopia development.[12]

An increased lag of accommodation has been found in both myopic children and adults when compared to other refractive groups in some studies[13-16] but not in others.[17-19] Goss[20] and Gwiazda *et al.*[21] found that accommodative responses were reduced before the onset on myopia, but Mutti *et al.*[22] found the increased lag was only present after the onset of myopia, and disputed the idea that an increased lag of accommodation caused myopia development. Allen and O'Leary[16] found that both an increased lag of accommodation and reduced accommodative facility were independently correlated with the progression of myopia over the following 12 months.

Recently the relationship between the treatment effect on the near focus and the resultant effect on myopia progression has been investigated by Berntsen *et al* [23] who found no significant association between lag of accommodation and myopia progression in their cohort aged 6-11 years, where lag of accommodation was manipulated using progressive addition lenses in 41 subjects over a 1 year period before reverting back to single vision lens wear. Previously the CLEERE study group had not found an association between lag of accommodation and annual myopia progression in their cohort.[24]

There is evidence that some types of retinal defocus are related to myopic progression. A clinical trial aiming to slow myopic progression using spectacle lenses that reduced peripheral hyperopic defocus, rather than foveal hyperopic defocus, showed that one of three experimental lens treatments had a small effect that was greater in younger subjects with parental myopia.[25] Myopia progression is, on average, greater in younger children and reduces with age.[26] In animal models, neonates show an increased response to image degradation when compared to older animals.[27]

The Cambridge Anti Myopia Study (CAMS) was designed to improve two accommodation functions. Treatment consisted of aberration control contact lenses to reduce lag of accommodation and vision training to increase accommodative facility. Whilst accommodative function can be improved through vision training[28-33] and manipulation of ocular aberrations[34,35] their effects on refractive error progression have not yet been established. The main outcome measures of CAMS were progression of myopia (assessed by cycloplegic auto-refraction) and axial length measurement (assessed by partial coherence interferometry). The treatment design, methods and outcome have already been published.[36] Overall there was no significant treatment effect .This paper assesses the interaction between treatment modality and age, on accommodative function and myopia progression, which were assessed at each of the follow up visits throughout the 2 year trial period. This paper aims to add to existing literature on variables associated with myopia progression.

Methods

The treatment modality for CAMS employed custom designed contact lenses to alter existing ocular spherical aberration, in an attempt to improve static accommodation responses during near-work, in conjunction with a vision-training program to improve accommodation dynamics. A factorial trial design was used to test the efficacy of the two independent treatments simultaneously. The clinical trial received ethical approval from the Anglia Ruskin University Research Ethics Committee and complied with the tenets of the Declaration of Helsinki.

Study Design

142 myopic subjects aged 14-22 years were recruited according to the following criteria:

- Spherical equivalent refractive error: -0.75 to –10.00 Dioptres
- Astigmatism: 0.75 Dioptres or less
- Zero or positive levels of spherical aberration at distance
- Corrected log MAR visual acuity: 0.00 or better in each eye
- No heterotropia or decompensated heterophoria (as assessed by cover test)
- Free of ocular pathology

- Free of systemic pathology which may affect myopia progression
- Able and willing to wear soft contact lenses for the duration of the trial

Informed consent was obtained from the subjects after explanation of the nature and possible consequences of the study.

Allocation of subjects to treatment group

One experimenter, who allocated subjects to the treatment group, did not take part 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. Masked experimenters had no information about the way individual subjects were allocated to treatment groups, and remained masked for the duration of the study.

Blocking variables were age, gender, and cylindrical refractive error and were stratified for spherical refractive error. All subjects wore contact lenses, either treatment or control, for the duration of the study.

Subject numbers for each treatment group are shown in Table 1. There was no significant difference between treatment groups in age (p=0.26), baseline refraction (p=0.45) or gender (p=0.93)

Table 1 here

Treatment design

(a) Altered spherical aberration

Soft contact lenses were designed to alter ocular spherical aberration in addition to correcting the spherical equivalent axial refractive error. All measures of spherical aberration throughout the study were referenced to a 5mm diameter pupil.

The front surface curvature was calculated using paraxial optics to correct the axial refractive error. The spherical aberration of the lens was manipulated by altering the eccentricity value of the front surface of the lens. The contact lenses were designed to alter the existing fourth order spherical aberration of the patient to -0.1 microns while maintaining the appropriate paraxial correction. Both the treatment and control group contact lenses were worn at least 10 hours per day. Compliance was assessed verbally by investigators at each follow up appointment. The contact lenses were usually replaced every 6 months on average, in some cases deposits were noted at the first 3 months check in which case, lenses were replaced every 3 months. Lenses were also replaced when a change of -0.25D or more was detected, or if lenses became damaged. Subjects were given a rub and rinse all in one solution to use.

(b) Vision training

The vision training regime consisted of lens flipper exercises[37] using a +2.00D/-2.00D flipper at 40cm. The exercises were performed for 18 minutes per day for up to six weeks. The subjects were instructed to wear their contact lenses during vision training and to complete a log book of their progress at the end of each training session.

The training was conducted at home with the log books randomly checked for training compliance by an unmasked examiner.

Procedures

Details of these methods have been published previously [36], but are presented here in brief.

Aberration measurement

The monochromatic wavefront aberration function of the eyes without correction was measured using the Complete Ophthalmic Analysis System (COAS),[38,39] at baseline, then with and without contact lenses at follow up visits. Aberration measurements obtained from 3 consecutive readings over a pupil diameter of 5mm were averaged.

Subjective refraction

Subjective refraction was performed to an accuracy of 0.12D before cycloplegia, to determine the paraxial power of the contact lens, the contact lenses were manufactured to an accuracy of 0.12D.

Accommodation Function Assessment

Accommodative response amplitudes were measured with an open field, infra-red Shin Nippon SRW 5000 auto-refractor.[40,41] Measurements were obtained from the left eye which was effectively occluded with an infra-red transmitting filter (Kodak Wratten 88A), whilst the right eye viewed the targets.

At baseline the accommodative stimulus values were adjusted to take account of ocular accommodative demand as the subjects' refractive errors were corrected with trial lenses.[14] At all subsequent visits the subjects wore their contact lenses, with any over-refraction corrected with trial lenses, during measurement of accommodative function.

(a) Monocular accommodative response amplitude to targets in real space.
Targets were presented in real space at distances of 6.00m, 0.40m, 0.33m and 0.25m. For 6.00m, the target consisted of a row of 6/7.5 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.

(b) Accommodative convergence to accommodation response (AC/rA) ratio
The subjective refraction of both eyes was placed in a trial frame for these measurements at baseline, and any over refraction placed over CAMS contact lenses at subsequent visits. The Shin Nippon auto-refractor was used to measure the accommodative response amplitudes (from the left eye) while concurrent vergence measurements were taken using a near Howell-Dwyer phoria card, positioned at 0.33m. The procedure was repeated using the near Howell-Dwyer card with supplementary lenses of power +2.00D, +1.00D, -1.00D and -2.00D added binocularly to the subjective refraction. Since there is measurement error and resulting variability in both the accommodation and convergence tests when measuring the response AC/A ratio the slope of the principal axis was calculated.[42,43]

(c) Monocular accommodative facility
The accommodative facility was measured at 6.00m and 0.40m for the right eye only with semi-automated lens-flippers interfaced with a computer.
Accommodative facility at 6m was measured using a Plano/–2.00D lens combination with the participant viewing 6/7.5 letters, while at 0.40m an N6 target was viewed through a flipper consisting of +2.00D/-2.00D lens combination. Distance

accommodative facility was measured before near facility.

Cycloplegic auto-refraction

Cycloplegic auto-refraction was used to determine change in refraction over the course of the trial. The refractive error of both eyes was determined following cycloplegia with two drops of Tropicamide Hydrochloride 1% (Minims; Chauvin) [44] Objective measurement was made by an unmasked observer with a Nidek AR600-A auto-refractor using a series of five readings per eye.[45]

Cycloplegic ocular biometry

Ocular dimensions of both eyes were measured under cycloplegia using an IOL Master (Zeiss Humphrey, CA, USA).

Statistical Methods

Step 1

An initial analysis of the data was performed using Partial Least Squares analysis (PLS). The reason for the PLS method is that in a situation with large numbers of variables with potential multicollinearity, in a relatively small sample size this analysis makes no assumptions about co-dependency and missing data[46,47] and therefore produces the least biased view of any relationships between ocular parameters measured.

PLS represents a multivariate analogue to multiple regression, where rather than examining a single y-variable against several x-variables, interest lies in the relationship between more than one y-variable (myopia progression for right and left eyes at different points in time) and several x-variables (remaining 29 measured variables at different points in time).

For its first component, PLS looks for a linear combination of the y's which has the highest correlation with a linear combination of the x's, and the first component explains as much of the original variation as possible; the second component explains as much of the remaining variation as possible, and the process is repeated until no additional variation can be accounted for. This process identifies variables that are most strongly associated with myopia progression over the trial duration.

Step 2

In order to identify the role of treatment groups over time, a Repeated-Measures

Analysis of Variance (ANOVA) was then performed, modelling progression in the right eye against the design factors:

1. Between subjects: Contact Lens (CL) group, Vision Training (VT) group and the interaction between CL and VT treatment.
2. Within subjects: Visit, and interactions between Visit and the between-subject effects.

Step 3

Variables identified in step 1 were then introduced sequentially into the model as follows:

1. Age effects: age of subject, and possible interaction between age and Contact Lens (CL) group;
2. Interactions between age, ACA ratio, lag of accommodation, CL group and VT group;

Step 4

Significant interactions identified in earlier steps, were explored further in sub-groups (of the treatment groups) using t-tests.

The PLS steps were performed using the SIMCA-P+11 statistical software; the, repeated-measures ANOVA and t-tests were performed using STATISTICA (version 8).

Results

As reported by Allen *et al* [36], there was no significant effect of either treatment on myopia progression in the overall study population, with myopia progression of -0.33D on average over the 2 years of the study. There was no significant treatment effect of either Vision Training or Contact Lens Spherical Aberration control on myopia progression. One hundred subjects completed the first 12 months of the trial, 95 subjects completed the total 24 month trial period. Loss to follow up is reported in Allen *et al.* [36] Mean baseline refractive error was -2.93D, SD 1.73D, range -0.75 to -8.02D.

The other major findings are summarised below before a more detailed statistical breakdown.

1. Vision training had no effect on progression, although all treatment groups showed increased accommodative facility over the trial period.

2. Altered spherical aberration by means of the contact lens treatment had the desired effect on lag of accommodation initially; however, effects were transient and had disappeared by the fifth visit at 12 months.

3. Over the two years, there was no difference in progression between experimental and control groups, however a more detailed analysis by age showed a significant difference in treatment effect between contact lens treatment groups in younger subjects, aged under 16.9 years (median age) at baseline

Change in spherical aberration as a result of contact lens treatment.

Both the treatment and control contact lenses produced their desired effects and are shown in Figure 1. The mean spherical aberration in the treatment group changed from +0.05µm ± 0.04 without the lenses to -0.11µm ± 0.05 with the lenses in situ. This difference was significant at all visits ($p< 0.001$). The control contact lenses had no significant effect on the spherical aberration of the control group (+0.07µm ± 0.04 without the lenses; +0.06µm±0.08 and with the lenses in situ; p=0.12). A repeated measures ANOVA showed no significant difference in spherical aberration of eye plus contact lens over the trial duration in either the CL treatment group ($F_{(2.7, 59.4)}=0.95$ p=0.42) or CL control group ($F_{(3.2, 107.1)}=0.92$, p= 0.44).There was no significant difference in spherical aberration of the eye only over the duration of the trial ($F_{(3.8,248.8)}=1.47$, p=0.21).

Figure 1. here

Step 1 Variables associated with myopia progression identified in the Partial Least Squares Analysis.

29 variables, including refraction, biometry and accommodation variables, measured at visits over the 2 years of the study were modeled against right and left eye progression over the study duration.

From the PLS results, numerically low values (indicating a negative, or more myopic shift in refractive error) for myopia progression, were most strongly associated with high values for Visit (i.e. as more time passed there was a greater amount of myopia progression), AC/A ratio (a higher AC/A ratio was associated with a greater amount of myopia progression), lag of accommodation at all tested distances (increased lag of accommodation was associated with a greater amount of myopia progression) and low values for age (younger subjects experienced greater amounts of myopia progression). The PLS analysis produced the Loadings Plot shown in Figure 2, accounting for 38% of the total variation. The relative position of the x's and y's on the Loadings Plot reflect the closeness of the relationships between the original variables, with those grouped together (or diametrically opposite) on the plot indicating high positive (negative) association.

As expected there was a high correlation between increase in axial length and increase in myopia progression ($r = -0.68$ $p < 0.001$). Hence results in this paper link to change in refraction only. Biometry details can be found in Allen *et al.* [47]

Figure 2 here

Step 2 Treatment group interactions

A two-way repeated measures ANOVA was used to check for any interaction between treatment regimens and change in refraction in the right eye. There was no interaction between contact lens treatment and vision training treatment at either 12 months ($F_{(1,123)} = 0.03$, $p = 0.86$) or 24 months ($F_{(1,113)} = 0.13$ $p = 0.72$). Hence, it was possible to investigate the two treatment options separately.

The repeated-measures ANOVA of myopia progression including only the design factors (Contact lens group, Vision Training group and Visit) highlighted significant differences between the overall means at each visit ($F_{(3, 258)} = 24.76$ $p < 0.001$), but no significance for the Contact Lens x Visit interaction ($F_{(3, 258)} = 2.25$ $p = 0.08$).

Step 3 Covariates

The Variables Age, ACA ratio and Lag of accommodation identified in the PLS analysis were entered as covariates in the repeated measures ANOVA.

Inclusion of age as a covariate indicated a significant overall effect on myopia progression due to subject age ($F_{(1, 258)} = 10.05$ $p < 0.001$), but also that this effect differed between the CL treatment groups due to a significant interaction between CL treatment group and age (*F* $_{(1, 258)}$ = 8.32 *p* = 0.01)

AC/A ratio was the only other significant covariate (*F* $_{(1, 252)}$ = 6.07 *p* = 0.01). As AC/A ratio increased, myopia progression increased. Lag of accommodation was not significant in the model (*p*>0.10).

No other significant interactions were found between other covariates (lag of accommodation and AC/A ratio) and CL treatment group, or between any of the covariates and VT treatment group.

Step 4 Further investigations of interactions

The age/contact lens treatment interaction determined previously was examined in more detail. In order to keep the group populations as large as possible, with an equal number of subjects, the cohort was divided into two age groups based on a median split of age in years at baseline (younger than 16.9 years and 16.9 years and older).

Figure 3 here

Figure 3 shows that in younger subjects there appeared to be a contact lens treatment effect over the first 12 months of the trial that was not present in older subjects. After this, between 12 and 18 months there was then an increase in myopia progression in younger CL treatment subjects whose myopia progression reached a similar level to younger CL control subjects at 18 months.

Due to the significant interaction between contact lens group and age group ($F_{(1,95)}$= 1.87, *p*=0.03) a two-way between-groups analysis of variance was conducted to explore the impact of contact lens treatment and age on change of refraction. At 12 months younger subjects in the CL treatment group had a significantly smaller change in refraction (-0.11± 0.29) than those in the contact lens control group (-0.35±0.31; *p*= 0.01). In older subjects the difference between contact lens treatment group (-0.16± 0.28) and contact lens control group (-0.05± 0.20; *p*= 0.17) was not significant.

By 24 months there was no significant interaction effect between contact lens group and age group ($F_{(1,90)}$ = 3.78, p = 0.25). The main effect for age ($F_{(1, 90)}$ = 4.43, p = 0.04) was deemed not significant in this case. The main effect for contact lens group was also not significant ($F_{(1, 109)}$ = 0.27, p = 0.60). This result indicates that the significant treatment effect in younger subjects was not maintained over the second year of the trial. In younger subjects the CL treatment group change in refraction at 24 months (-0.38 ± 0.39) was not significantly different from the contact lens control group (-0.4 ± 0.43; p = 0.68). In the older age group, although there was increased myopic change in refraction in the CL treatment (-0.31 ± 0.27), this was not significantly different from the CL control group (-0.19D ± 0.24; p = 0.13).

In an attempt to explain the significant treatment effect noted in younger subjects, variables associated with myopic progression in the preliminary PLS analysis (Step 1) were investigated further.

a) Lag of accommodation

There was no significant difference in lag of accommodation at baseline between younger and older subjects (p=0.09).

There was a significant reduction in lag of accommodation in the CL treatment group at 3 months (p=0.001).[35] When split by median age group the reduction in lag of accommodation at 3 months was significant in younger CL treatment subjects (0.39 ± 0.68; p= 0.03), but not in older CL treatment subjects (0.28± 0.98; p= 0.14) subjects. The measured lag of accommodation at each visit is plotted in Figure 4.

Figure 4 here

Figure 4 demonstrates the initial successful reduction in lag of accommodation from baseline by the CL treatment at 3 months. However after this time point there is an increase in lag of accommodation over the duration of the trial.

b) AC/A ratio

Inclusion of additional measurements highlighted accommodative convergence to accommodation ratio (AC/A) as the only other significant covariate (p= 0.01). No further improvement to the model was achieved by including the interactions between these measurements and the CL group, or by the interactions between these measurements and subject age. After Bonferroni correction there was no significant difference between AC/A ratios in CL and VT treatment groups at any visit during the trial. No interaction was found between AC/A ratio and age, indicating a similar pattern of change in AC/A ratio in treatment groups over time in each age group. AC/A ratio in each CL and VT treatment group over the trial duration are reported in Table 2.

Table 2 here

In light of previous associations between treatment effects and near esophoria[48,49] we investigated the contact lens treatment effect in those with esophoria at near at baseline (n= 21).There was no significant difference in myopia progression between contact lens treatment groups at 12 months and 24 months (p= 0.47 and p= 0.54 respectively) in subjects with near esophoria.

Effect of Vision Training

Facility of accommodation during the course of the trial was not significantly associated with myopia progression. Moreover there was no treatment effect of vision training on myopia progression. At 3 months there was a significant increase in near accommodative facility rate in the VT treatment group but not in the VT control group.[35] Over the duration of the trial, facility of accommodation improved in both VT treatment and control groups (Table 3) by very similar amounts. There was no significant difference with regards to change in facility rate between VT treatment groups (distance or near) at 12 months or 24 months (p>0.09 in all cases).

Although only near facility was trained, there was an increase in facility rate at both distance and near. Data for accommodative facility rates are presented in table 3 for subjects who attended baseline, 12 and 24 months visits.

There was no interaction between accommodative facility change and age (p=0.69). Accommodative facility rate and facility training were not significantly associated with myopia progression.

Table 3 here

Discussion

The CAM study, which includes active interventions to alter accommodative lag and facility, shows that in a multifactorial model, AC/A ratio and lag of accommodation are significantly correlated to myopia progression confirming earlier observations by Mutti *et al.* [50] and Gwiazda *et al*.[21]

The aim of the CL treatment was to reduce lag of accommodation, which has been implicated in previous work as a factor influencing myopia progression.[15,16] Our results indeed show that CL treatment group had a reduction of lag of accommodation during the initial stages of treatment. This was especially pronounced in younger subjects.

Lag of accommodation had increased at the end of the trial in CL treatment and CL control groups. Despite the carefully controlled approach to accommodation measurement, it is possible that familiarization or repeated measurements of accommodation affected subject performance. A small increase in measured lag of accommodation was also noted over the duration of the STAMP trial,[23] although not of the same magnitude as in this study.

There was significantly less myopia progression with aberration control contact lenses in the younger half of our cohort over the first year of treatment; however progression increased in the second year of treatment, especially between 12 and 18 months. The significant treatment effect at 12 months should be considered cautiously, as there was no significant difference in treatment groups prior to this point, possibly because of low myopia progression during this time.

The regression after 12 months could be due to the lag of accommodation returning to pre-treatment levels.[51] Inducing negative spherical aberration produces a sustained reduction in lag of accommodation for up to three months,[34,35] but our results show that the effect wears off after approximately one year. Although adaptation effects may be a factor, there appears to be a general trend for lag of accommodation to increase in all groups over time.

Despite an initial reduction of accommodative lag in older subjects in the contact lens treatment group, they showed no reduction in myopia progression compared to the control group.

The finding of a significant treatment effect in younger subjects has also been recently reported when using a novel spectacle lens design to reduce peripheral hyperopic defocus.[25] Because younger subjects tended to show a greater progression rate than older subjects in this study, we can presume that they are more susceptible to myopigenic stimuli. Hence we can suggest that younger subjects respond better to reductions in myopigenic stimuli (such as the reduction in lag of accommodation induced by the treatment contact lenses in this study).
Variations in pupil size may have altered the levels of spherical aberration which subjects experienced. Mean pupil diameter was 5.08mm (SD 0.83) which indicates that the actual spherical aberration would have been very close to desired levels. Subjects wearing the treatment contact lenses would experience -0.1 µm of fourth-order spherical aberration referenced to a 5 mm diameter pupil, but this would vary from -0.04 µm to -0.2 µm for pupil diameters of 4mm to 6 mm. These values approximate to -0.55 and -1.23 D respectively of spherical aberration at the edge of the pupils, so subjects would still experience negative spherical aberration compared to the control group.[36] Since pupil size varies throughout the day the aberration correction provided by the contact lenses in the CL treatment group is unlikely to have remained consistent throughout the day, but it is expected that the subjects would still have experienced negative spherical aberration.

Measuring accommodative lag through aspheric contact lenses could potentially affect the output of the autorefractor. However in the present study, measurements of accommodative lag were obtained by subtracting the resting state refraction from the refraction in the accommodated state. Since these measurements were both taken with the autorefractor through the same lens, the potential error in measurement from the aspheric contact lenses would be the same in all the accommodation measurements and be cancelled out by the calculation. We did not use our aberrometer to measure lag, as our instrument did not have an internal accommodative target; in addition lag of accommodation measurements with internal accommodative targets are often affected by proximal accommodation.

In an earlier study of correlations between accommodative functions and myopia progression in young adults, Allen and O'Leary[16] found that lag of accommodation and accommodative facility were significantly correlated with the 12-month change in myopia. While the AC/A ratio was significantly correlated with progression in a single factor analysis, it did not correlate significantly with progression in Allen and O'Leary's multifactorial model. Sample size, outliers or different age profiles might explain the differences in findings between the studies.

In the present study, facility of accommodation was not significantly correlated with myopia progression through the course of the study. Facility of accommodation improved markedly from baseline in the vision training treatment group, however there was an almost equally large improvement in the facility of accommodation in the control group. Siderov [52] noted that even a few measurements of accommodative facility may improve facility rates, and it may be that our regular measurements of facility rate in controls were almost as effective at improving facility as was the full vision training regime. The present study shows that the improvements gained through training or repeated testing were sustained over the 6 months between visits, and over the 2 year trial period. There was no interaction of age with vision training effect, indicating that accommodative facility training is suitable for increasing accommodation dynamics in the range of ages in this study.

It is noteworthy that the average rate of progression of myopia in this study was only $-0.17D.y^{-1}$.Because of the increase in accommodative facility across all subjects we cannot rule out the possibility that an improvement in accommodative facility is effective in reducing rates of myopia progression. It remains possible that the improvement of facility in both treatment and control groups in the present study might be responsible for the lower progression rates of subjects. However the lack of a significant interaction between progression of myopia and accommodative facility in the statistical analysis makes this unlikely. Rather, it suggests that the relationship previously found between myopia progression and accommodative facility[16] was not a causal one.

Peripheral retinal blur has been indicated as a potential stimulus to myopia progression.[53,54] No difference between peripheral refraction profiles were found between treatment groups in an increased CAMS cohort including subjects with negative spherical aberration at baseline,[55] suggesting that peripheral defocus was not a factor in progression differences seen between treatment groups in this study.

In the younger subjects in this cohort we have seen a reduction in lag of accommodation prior to a reduction in myopia progression. This finding offers support to the hypothesis that if focusing errors at near are reduced this may have an impact on myopia progression for a limited period of time.

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Figure 1. Spherical aberration of eye plus contact lens, in each CL treatment group and the cohort uncorrected (eye only) over the duration of the study. Error bars indicate standard error of the mean.

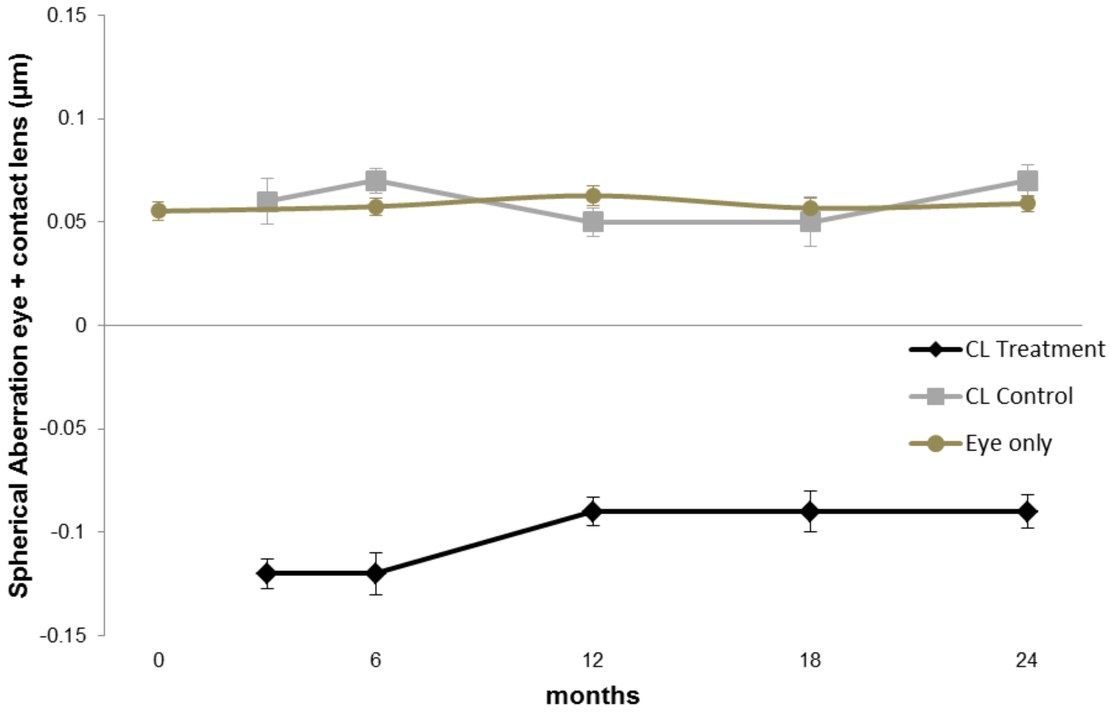

Figure 2. Loadings Plot from Partial Least Squares Analysis (NB- for clarity, only those effects which are significant are shown in the plot). Points clustered together are highly correlated. Points that fall on opposite sides of the origin exhibit negative correlations to one another

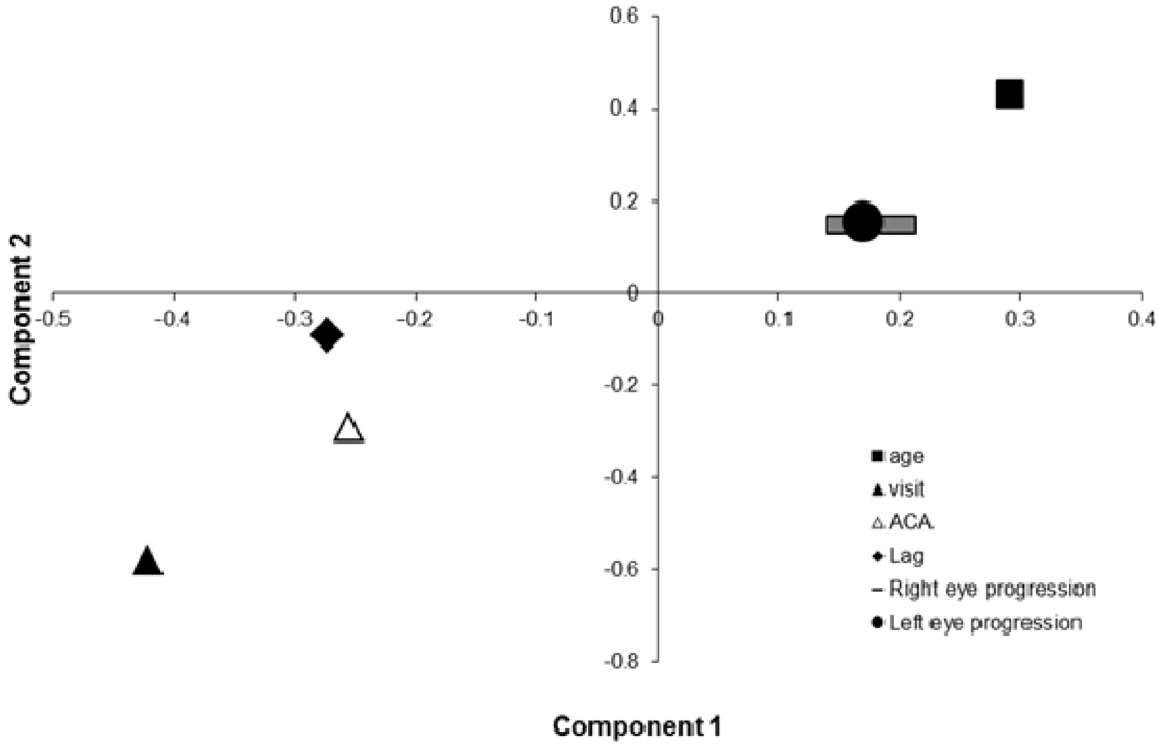

Figure 3. Younger and older CL and control groups change in refraction over the 2 year trial period. * denotes a significant difference (p= 0.005) in myopia progression at 12 months between CL treatment and CL control in younger subjects (aged less than 16.9 years). Error bars indicate standard error of the mean.

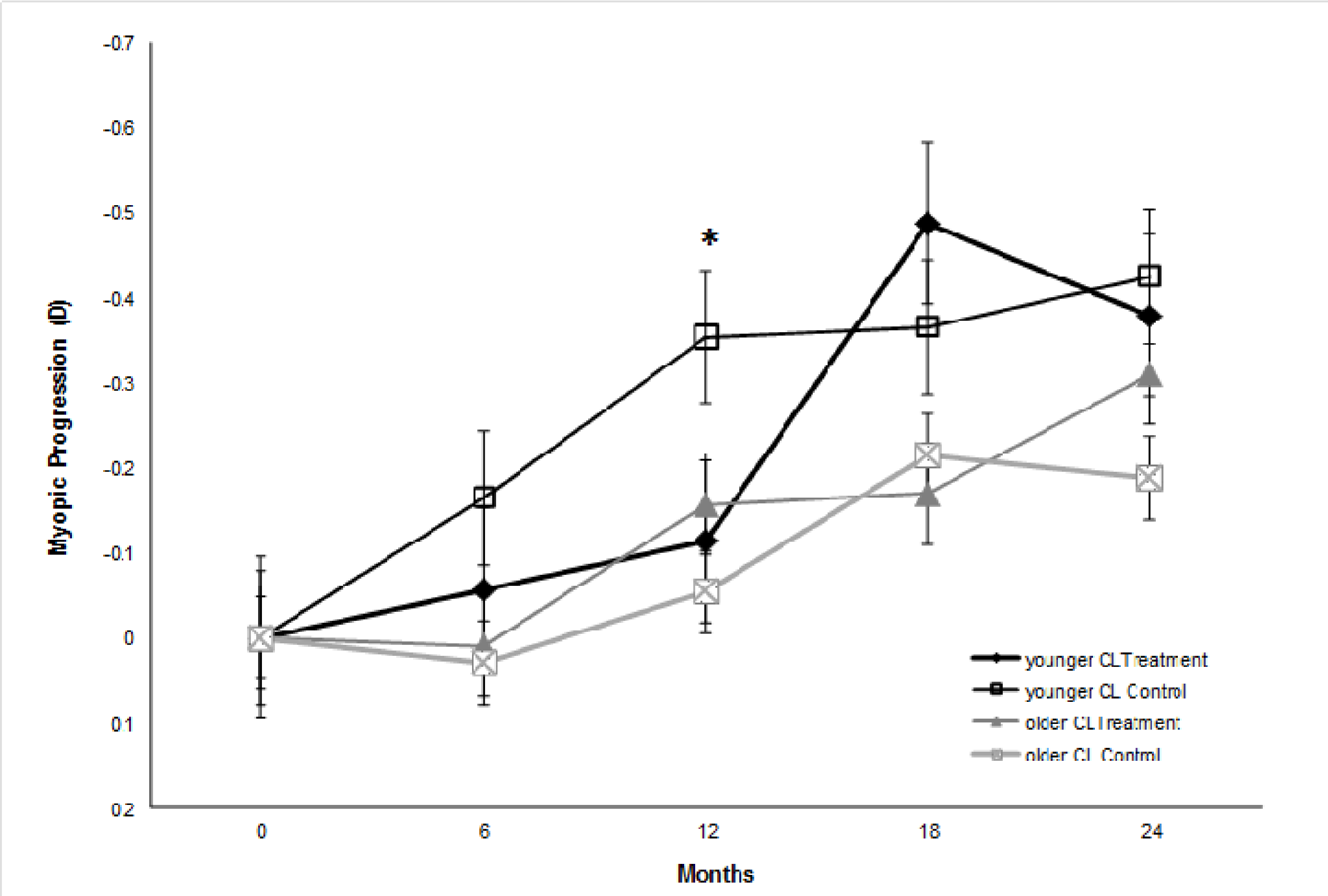

Figure 4. Measured lag of accommodation at each visit for subjects split by age and CL treatment group. Error bars indicate standard error of mean. * indicates a significant difference in lag of accommodation between younger CL treatment group and younger CL control group (*p*=0.03)

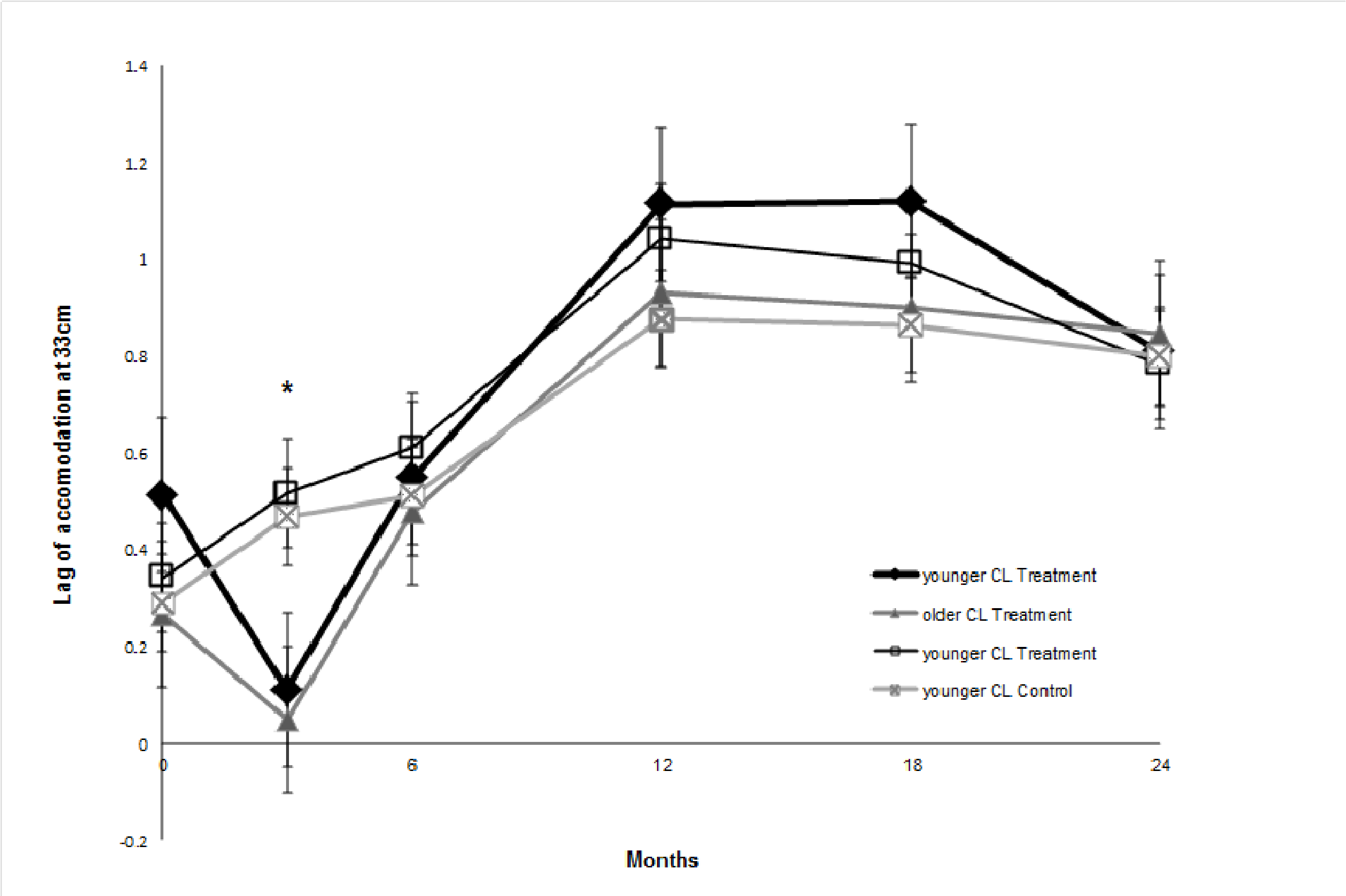

Table 1

Treatment groups, subject numbers and age ± 1 standard deviation at baseline. SE = Spherical equivalent

altered spherical aberration and vision training (CL1+VT1) n=25 mean age 16.72 ± 2.3 mean SE -2.49D ±1.5	vision training only (VT1) n=31 mean age 17.39 ± 2.39 mean SE -2.81D ± 1.81
altered spherical aberration only (CL1) n=41 mean age 16.29D ± 2.23 mean SE -3.16 ± 1.68	unaltered spherical aberration and no vision training (CL0+VT0) n=45 mean age 16.69D ± 2.23 mean SE -3.03 ± 1.84

Table 2

AC/A ratio ± 1 standard deviation, average over the 2 year trial duration in subjects completing the trial. CL=Contact Lens VT=Vision Training.

Treatment Group	n	AC/A Ratio ± 1SD
CL Treatment + VT Treatment	16	4.44 ± 2.4
CL Treatment +VT Control	29	4.17 ± 2.0
CL Control +VT Treatment	20	4.53 ± 1.5
CL Control + VT Control	30	4.02 ± 1.33

Table 3

Facility rates at distance and near for vision training (VT) treatment and control groups, over the duration of the trial. (1 VT control subject had missing facility rate data at 24 month visit).

Visit	Distance Facility rate (cpm) ± 1 S.D.		Near Facility rate (cpm) ± 1 S.D.	
	VT Treatment	VT Control	VT Treatment	VT Control
Baseline	14.2 ± 5.3 n=56	12.9 ± 5.0 n=86	14.1 ± 4.0	13.7 ± 4.4
12 months	18.8 ± 7.0 n=38	16.8 ± 5.2 n=60	16.9 ± 5.9	15.2 ± 5.5
24 months	21.6 ± 6.2 n=36	18.9 ± 5.9 n=58	19.2 ± 5.9	18.0 ± 5.6