Poster #30

The Accommodation Response in Marmosets with Imposed Anisometropia

Elise Harb, Sanbrita Ghosh, Kristen Totonelly, Mark O'Connor, David Troilo
New England College of Optometry, Boston, MA 02115

Introduction

• Imposing anisometropia in marmosets with monocular contact lenses or binocular contact lenses of opposite sign results in un-yoked compensatory changes in axial growth and refractive state (Troilo et al., 2007).

• In general, the accommodative behavior under anisometropic conditions is open to speculation. Flitcroft (1992) suggested that the accommodative demand between the two eyes was averaged to produce a consensual accommodative response. Hung (1995) hypothesized that the eye with the less demand was used to drive the accommodative response.

Purpose

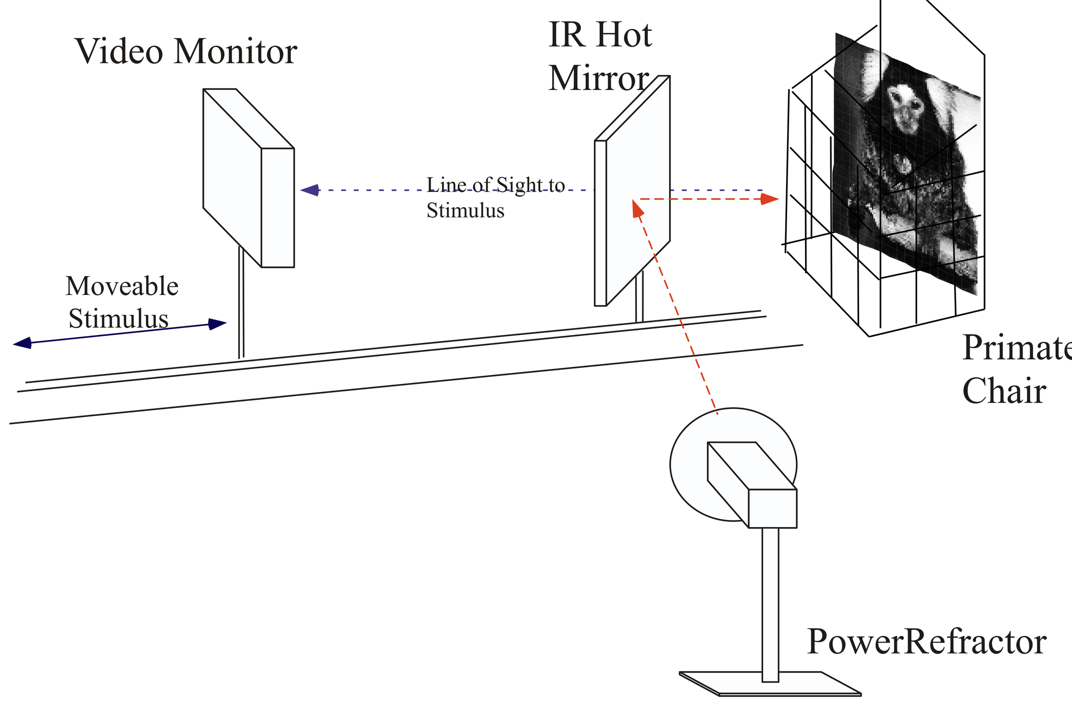
• In this study we attempt to describe the binocular accommodative response with lens imposed anisometropia in order to fully understand the effective refractive state experienced during such lens wear.

Methods

• We measured binocular accommodation in three untreated marmosets (ref. error range: +0.75 to -1.30) binocularly fit with custom made soft contact lenses to produce three anisometropic conditions;(1) pl/+3, (2) pl/-3, (3) +3/-3. The lenses were worn for only the period of time needed to measure accommodative function (approx 30 min).

Juvenile marmosets wearing soft contact lenses.

•The binocular accommodative response was measured through each of the anisometropic conditions and with no lenses with an IR videorefractor (PowerRefractor, MultiChannel Systems) on multiple occasions at varying accommodative stimuli positions.

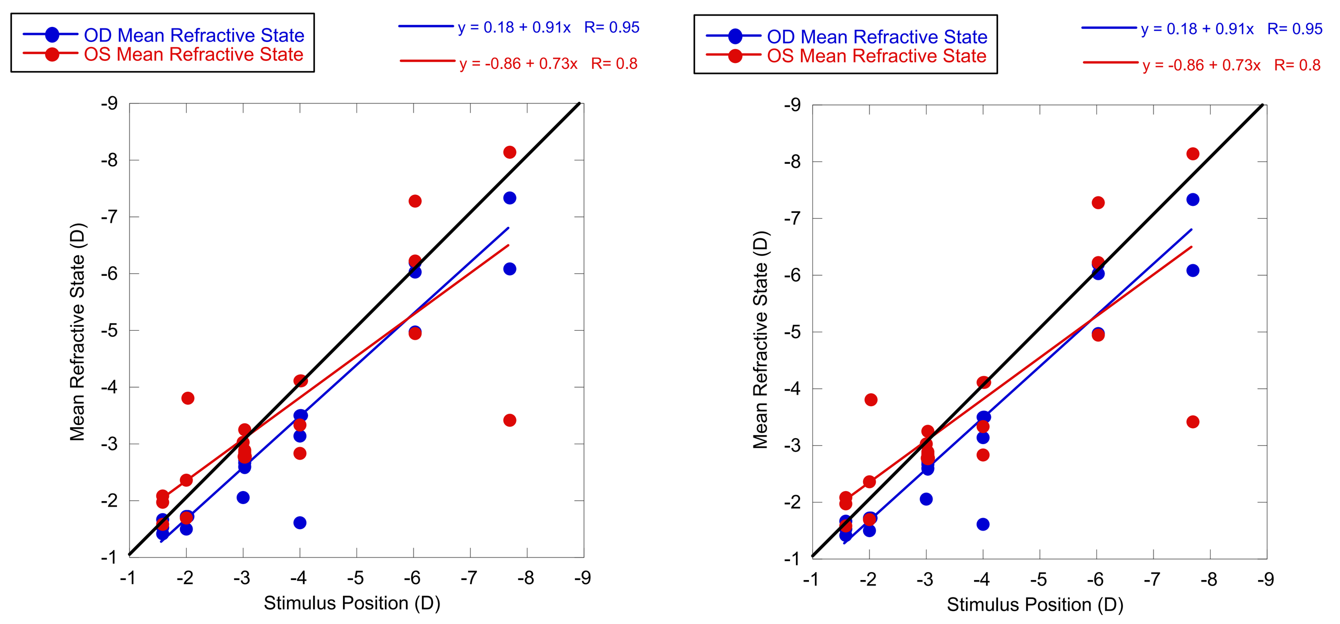


• Visual stimuli consisted of video images displayed at varying distances (between 0.50 and 0.13 m) from a primate chair. The PowerRefractor was used to monitor eye position and refractive state continuously (Schaeffel et al.,1993).

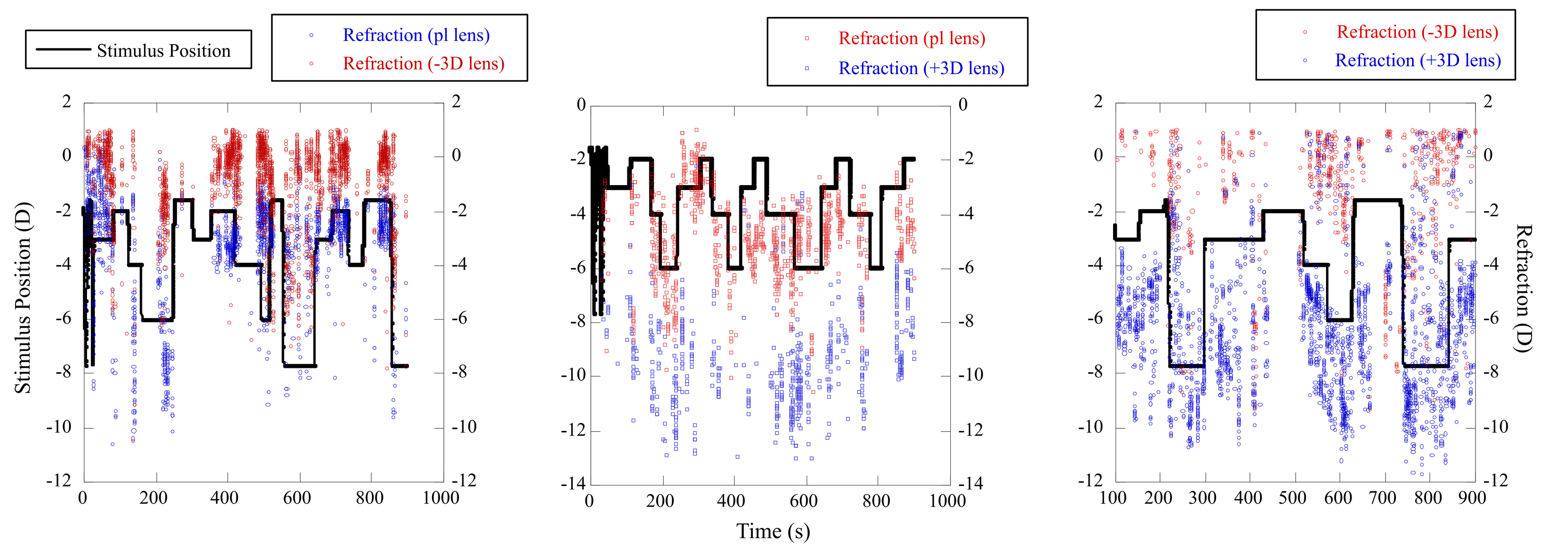
• Accommodative stimulus demands were calculated from the target distance, subjects' cycloplegic refraction (measured on another day) and lens power worn.

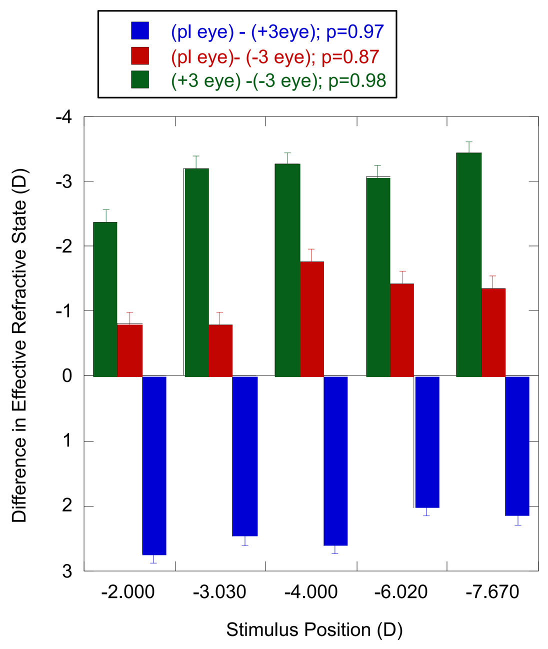
Results

• Two subjects measured with no lenses in place demonstrated appropriate shifts in refractive state for changing stimulus positions, as shown by the stimulus-response functions below.



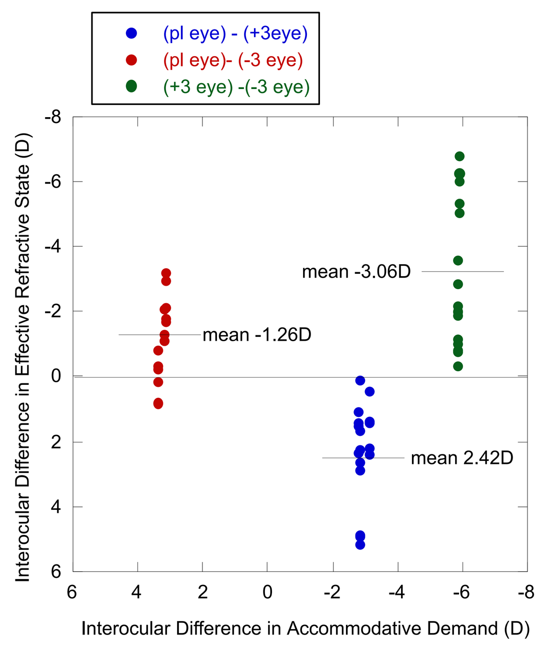
• Examples of accommodative changes under lens-imposed anisometropic conditions, suggest that the relatively more myopic eye was better focused to the stimulus.

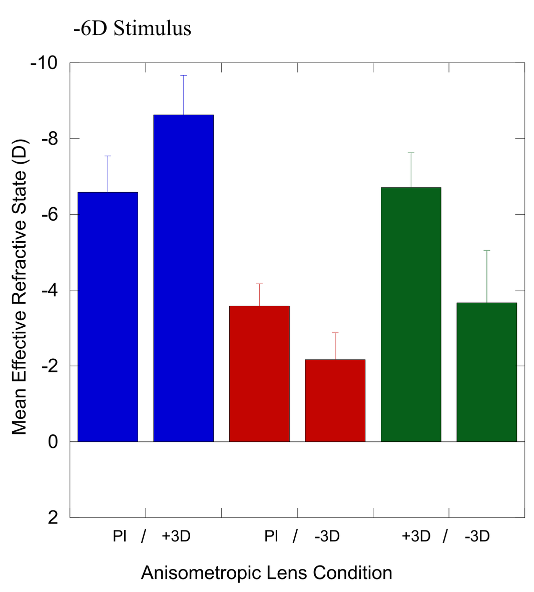




• The difference in the effective refractive state between the two eyes differed consistently between lens conditions at all stimulus positions.

• Although the imposed anisometropic conditions created expected differences in accommodative demand between the two eyes, the mean difference in the response was always less than the demand difference when a negative lens was worn.





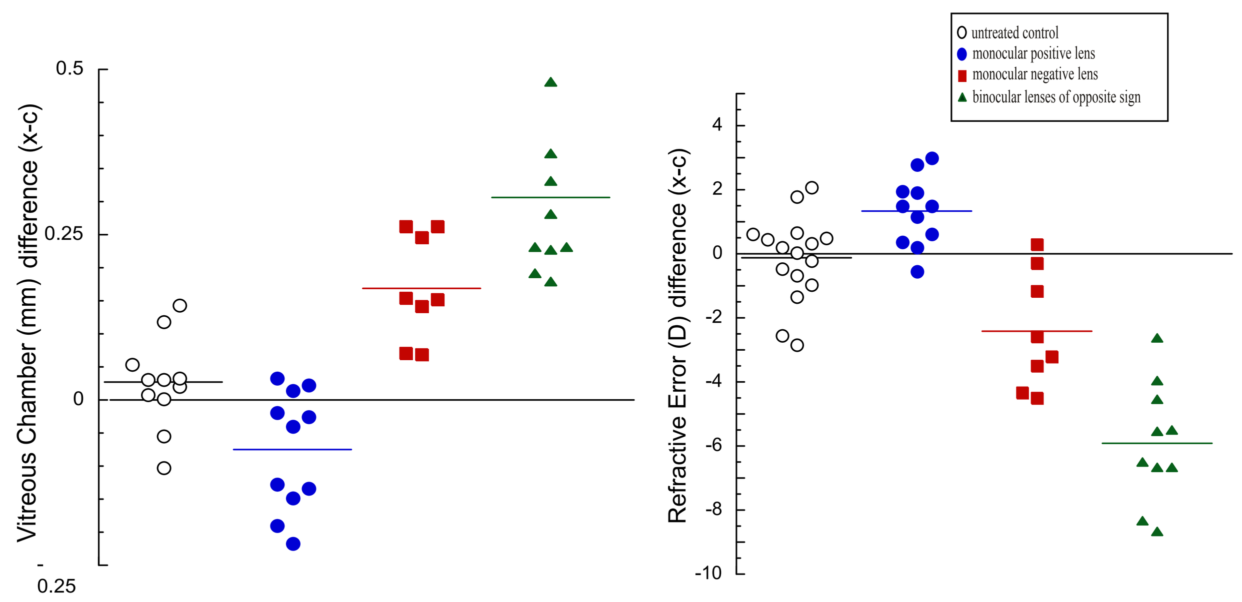
• Examples of the refractions at the 6D stimulus distance suggest that the presence of a negative lens produces a reduced accommodative response in the contralateral eye suggesting that the accommodative demands are averaged between the two eyes in these conditions.

Summary and Conclusions

• Under lens imposed anisometropia, it appears that the accommodative demand of each eye is providing input into the accommodative response, potentially by an averaging mechanism.

• It appears that the presence of a negative lens decreases the accommodative response of the contralateral eye, potentially by increasing the average accommodative demand of the two eyes.

• In general, the accommodative errors experienced by each eye under the three anisometropic lens conditions result in retinal defocus conditions that predict the compensatory growth patterns observed in marmosets, as described earlier (Troilo et al., 2007);



· pl/+3: +3 eye experiences more myopic defocus and becomes relatively more hyperopic

· pl/-3: -3 eye experiences more hyperopic defocus and becomes relatively more myopic

· +3/-3: -3 eye experiences more hyperopic defocus and becomes relatively more myopic.

References

Flitcroft, D. I., Judge, S. J., & Morley, J. W. (1992) Binocular interactions in accommodation control: Effects of anisometropic stimuli. Journal of Neuroscience, 12(1), 188-203.

Hung, L., Crawford, M. L. J., & Smith, E. L. (1995) Spectacle lenses alter eye growth and the refractive status of young monkeys. Nature Medicine, 1(8), 761-765.

Schaeffel, F., Howland, H., Weiss, S. & Zrenner, E. (1993) Measurement of the dynamics of accommodation by automated real time photorefraction. Invest. Ophthalmol. Vis. Sci. (ARVO Suppl.) 34:1306.

Troilo,D., Totnelly, K., Kee, C-S., & Nickla,D. (2007) Aniso conatct lens rearing induces anisometroipa in marmosets. Invest. Ophthalmol. Vis. Sci. (ARVO Suppl.) 48:1032.

E. Harb Commercial Relationships: None
Supported by NEI-EY 011228
harbe@neco.edu

IS DOPAMINE A BIDIRECTIONAL EYE GROWTH REGULATOR?

THE AUSTRALIAN NATIONAL UNIVERSITY

Poster #35

VISION SCIENCE
ARC CENTRE OF EXCELLENCE

SIOBHAN McCARTHY[1], RYAN TAYLOR[1], PAM MEGAW[2], IAN MORGAN[1].

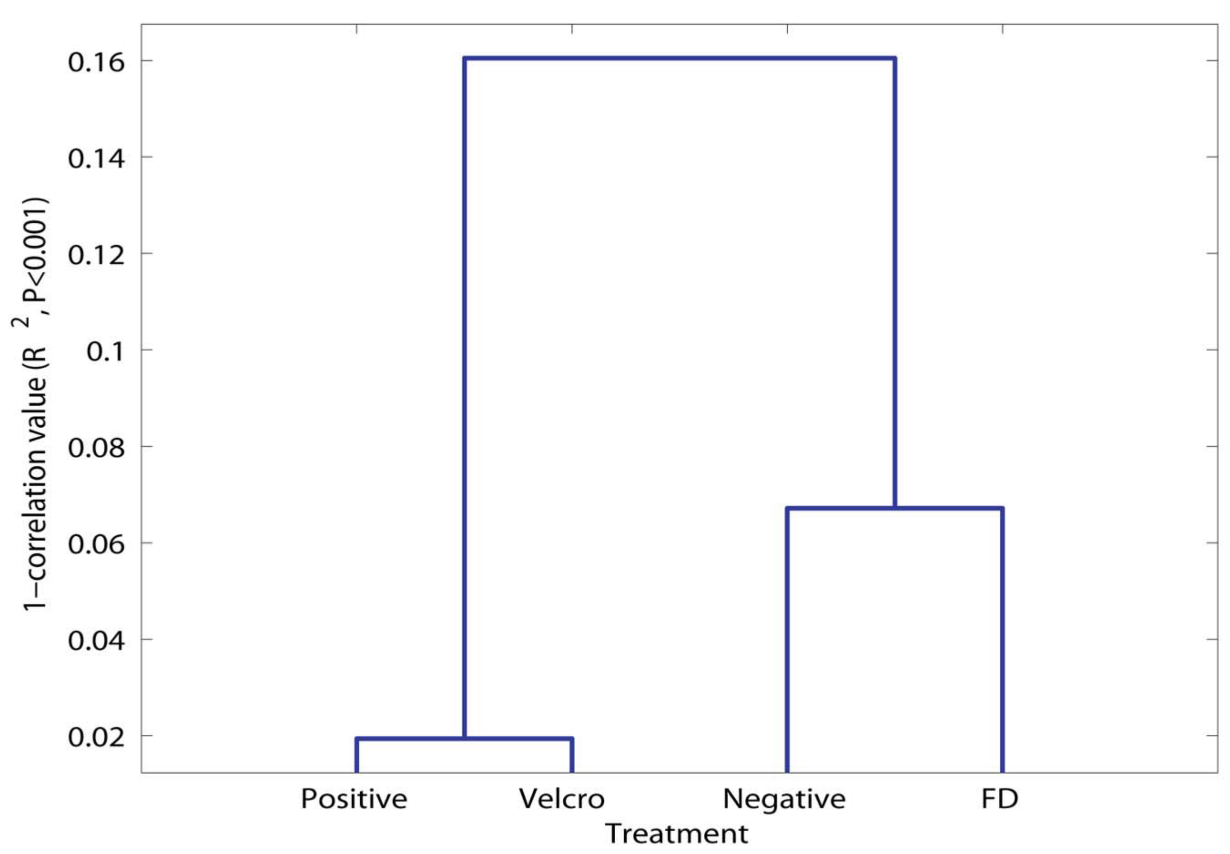
(1) ARC CENTRE OF EXCELLENCE IN VISION SCIENCE, RESEARCH SCHOOL OF BIOLOGICAL SCIENCES, AUSTRALIAN NATIONAL UNIVERSITY, CANBERRA, ACT AND (2) SCHOOL OF VETERINARY AND BIOMEDICAL SCIENCES, JAMES COOK UNIVERSITY, TOWNSVILLE, QLD.

AIM: To examine if retinal dopamine is a bidirectional eye growth regulation molecule. The hypothesis: If dopamine is involved in both growth promotion and inhibition retinal dopamine release should behave in an opposite manner under different eye growth paradigms.

METHODS: Chickens were fitted with diffusers, +10D or -10D lenses or Velcro mounts. On day 1 and 7 of treatment, vitreous samples were taken at 0 (dark), 2.5, 6 & 12 hours after lights on. Vitreal DOPAC accumulation was measured by HPLC-ED. R values were computed between each function (pmoles of DOPAC per vitreous over time) in eyes covered by each type of occular device to determine which treatments were most similar.

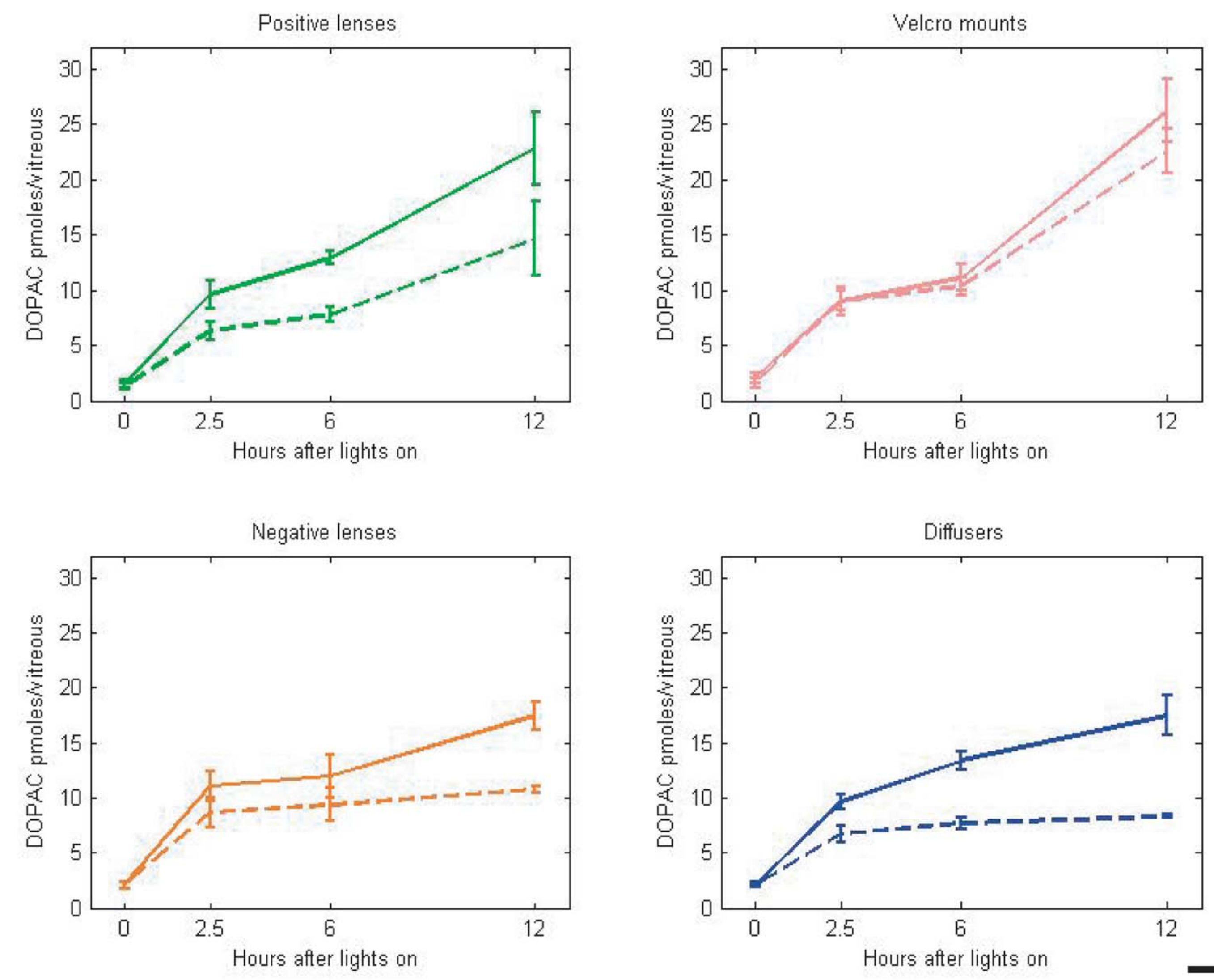
RESULTS: Vitreal DOPAC was reduced in chickens fitted with +10 lenses, minus lenses or diffusers over the light phase on both days 1 and 7 to a similar extent. However, there appeared to be some subtle differences in time-course, with the curves of the diffusers and -10D lenses groups appearing to plateau after about 6 hours, whereas accumulation of DOPAC continued with Velcro mounts and +10 lenses.

Similarities between patterns of vitreal DOPAC accumulation over time

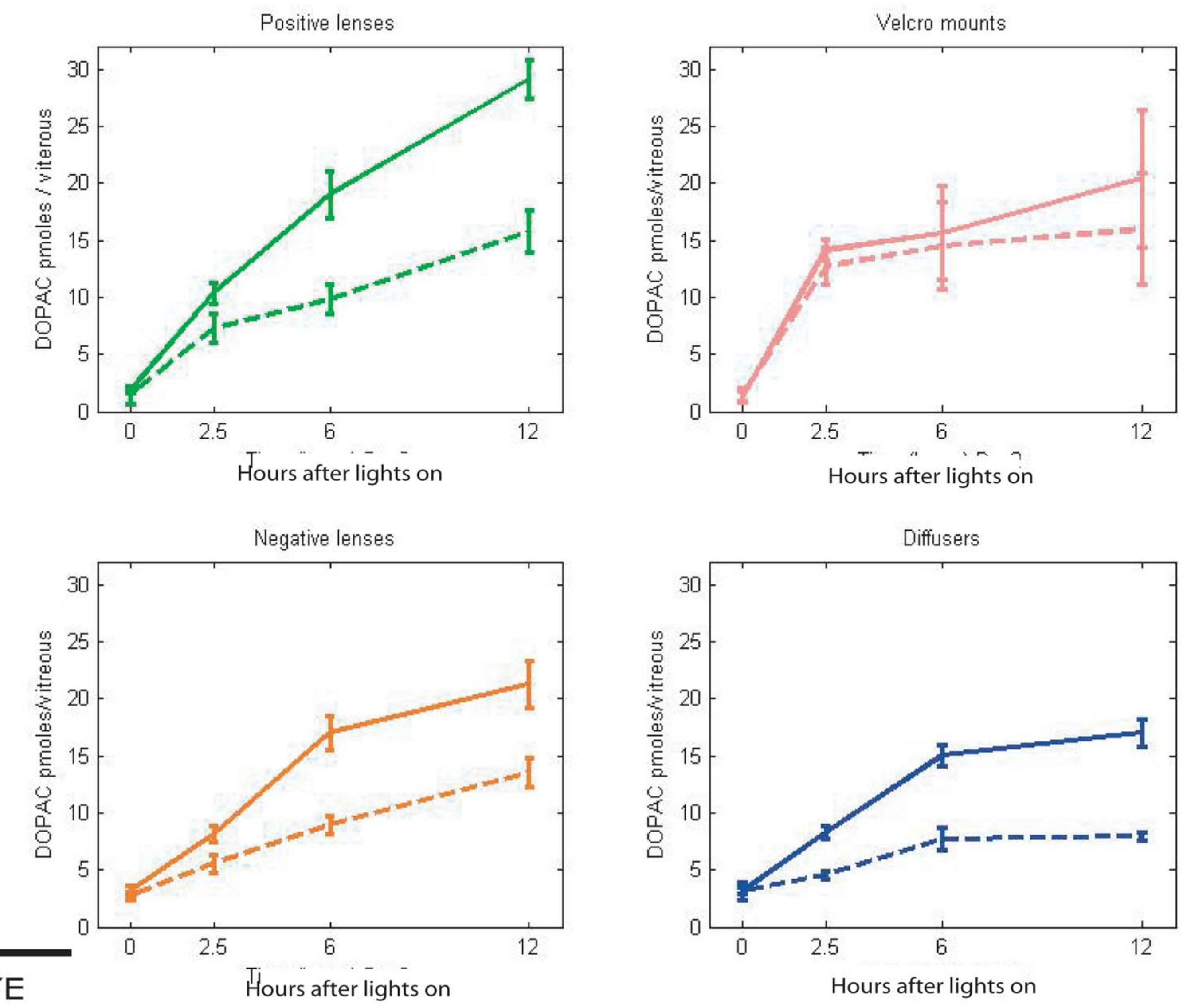


More detailed statistical analysis showed that positive lens and control treatments produce average time courses (over both days) that are more highly correlated (R^2=0.98, (1- R^2)=0.02, P<0.0001) with each other than either time course is with negative lenses or diffusers. In turn, negative lenses and diffusers are more highly correlated (R^2=0.93, (1- R2)=0.07, P<0.0001) with each other than they are with both positive and control lenses (R^2=0.84, (1- R^2)=0.16, P<0.05).

On the first day of occular device wear



After 7 days of occular device wear.



CLC EYE

Treated EYE

So are the kinetics of dopamine release different between positive lenses and negative lenses / diffuser?

The rate of influx of DOPAC into the vitreous, which is proportional to the rate of dopamine release can be determined by the equation:

$$n(t) = \frac{a}{k} + \left(n(0) - \frac{a}{k}\right) e^{-kt}$$

Where: *t* is time (in hours),
n(*t*) is DOPAC at time *t* (in pmol/vitreous),
k is the time constant for DOPAC efflux (per hour) and
a is the rate of influx of DOPAC into the vitreous (in pmol/hour),
which is proportional to the rate of dopamine release

	a (pmol/h)
Control (Megaw et.al, 2006)	4.13
Control - dark (Megaw et.al, 2006)	1.07
Control (Megaw et.al, 2001)	6.8
Control	4.6
Controlateral control eyes	
Positive lens CLC	3.9
Velcro CLC	6.63
Negative lens CLC	3.56
Diffusers CLC	3.78
Experimental eyes	
Positive lens	2.01
Velcro	5.51
Negative lens	1.34
Diffusers	1.96

Megaw, P.L., et al., *Diurnal patterns of dopamine release in chicken retina*. Neurochemistry International, 2006. 48(1): p. 17-23.
Megaw, P.L., et.al., *Vitreal dihydroxyphenylacetic acid (DOPAC) as an index of retinal dopamine release*. J Neurochem, 2001. 76(6): p. 1636-44.

SUMMARY:

- Dopamine is not a bi-directional modulator of eye growth.
- However, the kinetics of dopamine release during growth suppression appears to be different from kinetics of dopamine release during growth promotion… Is this important?
- Dopamine may not be a driver in the eye growth regulation pathway, but dopamine release may need to be reduced for experimental myopia to be induced.

Poster #53

Singapore National Eye Centre
A member of SingHealth

2 Years Follow-Up Results of Visual Acuity and Contrast Sensitivity Enhancement in Patients with Low Myopia using NeuroVision's Neural Vision Correction™ (NVC™) Technology

Singapore Eye Research Institute

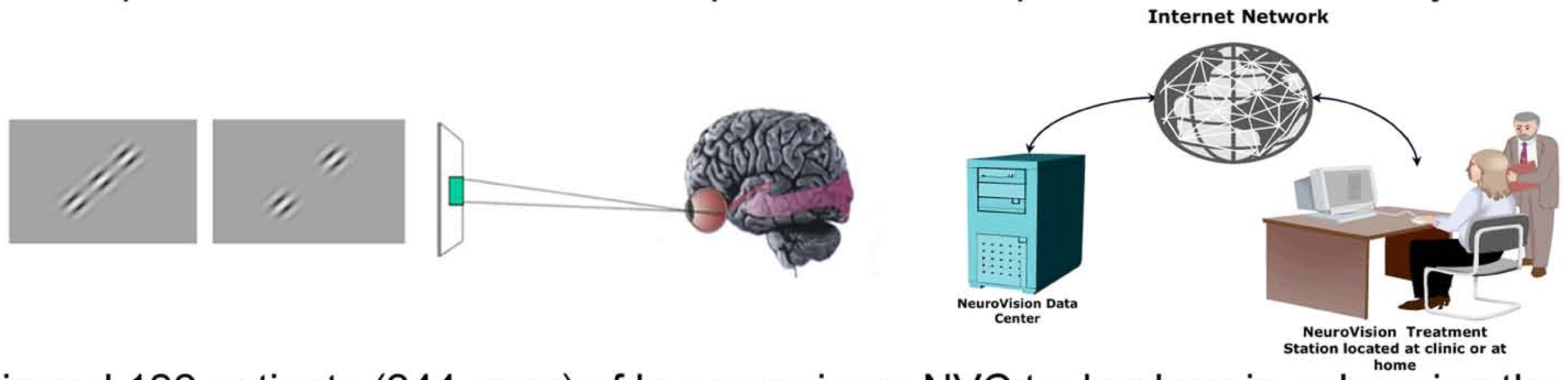
NUS National University of Singapore

Kalin Siow,[1,2] Donald T.H. Tan[1,2,3]

[1]Singapore National Eye Centre, [2]Singapore Eye Research Institute, [3]Dept. of Ophthalmology, Yong Loo Lin School of Medicine, National University of Singapore

Introduction

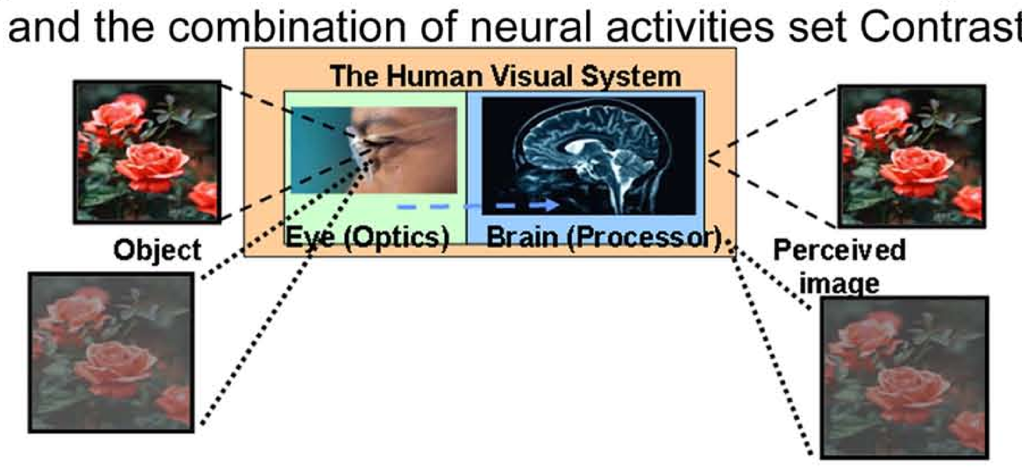
NeuroVision™ NVC vision correction technology is a non-invasive, patient-specific treatment based on visual stimulation and facilitation of neural connections responsible for vision. The technology involves the use of an internet-based computer generated visual training exercise regime using sets of patient specific stimuli based on Gabor patches, to sharpen contrast sensitivity and visual acuity.



We reviewed 122 patients (244 eyes) of low myopia on NVC technology in enhancing the unaided visual acuity (UAVA) and unaided contrast sensitivity function (UACSF) in low myopic patients with -1.50 D sphere and below and cylinder -0.75D or less. We also monitored the persistence follow-up to 24 months.

Scientific background

Cortical neurons in the visual cortex function as highly specialized image analyzers or filters, responding only to specific parameters of a visual image, such as orientation and spatial frequency, and visual processing involves the integrated activity of many neurons, with inter-neural interactions effecting both excitation and inhibition[1]. Visual contrast activates neurons involved in vision processing, and neural interactions determine the sensitivity for visual contrast at each spatial frequency, and the combination of neural activities set Contrast Sensitivity Function (CSF)[1,2].



Studies have shown that the noise of individual neurons can be brought under control by appropriate choice of stimulus conditions, and CSF can be increased dramatically through control of stimulus parameters[4-8] This precise control of stimulus conditions leading to increased neuronal efficiency is fundamental in initiating the neural modifications that are the basis for brain plasticity[9,10]. Brain plasticity (the ability to adapt to changed conditions in acquiring new skills) has been demonstrated in many basic tasks, with evidence pointing to physical modifications in the adult cortex during repetitive performance[11-12].

NeuroVision's technology probes specific neuronal interactions, using a set of patient-specific stimuli that improve neuronal efficiency[6,13] and induce improvement of CSF due to a reduction of noise and increase in signal strength. As visual perception quality depends both on the input received through the eye and the visual cortex processing, NeuroVision's technology compensates for blurred (myopic) inputs, coming from the retina, by enhancing neural processing. It does not reduce myopia.

Purpose

NeuroVision's NVC™ technology is a non-invasive, patient-specific, perceptual learning program based on visual stimulation and facilitation of neural connections at the cortical level, involving a computerized visual training regime using Gabor patches, to improve contrast sensitivity and visual acuity. We report the treatment in enhancement of unaided visual acuity (UAVA) and unaided contrast sensitivity function (UACSF) in low myopes and monitored the persistence of the improvement for up to 24 months.

Methods

244 eyes of low myopes (range 0D to -2.63D with spherical equivalent) underwent NVC treatment in Singapore National Eye Centre. 136 eyes completed 6 months follow-up, 54 eyes completed 12 months follow-up and 36 eyes completed 24 months follow-up post treatment end.

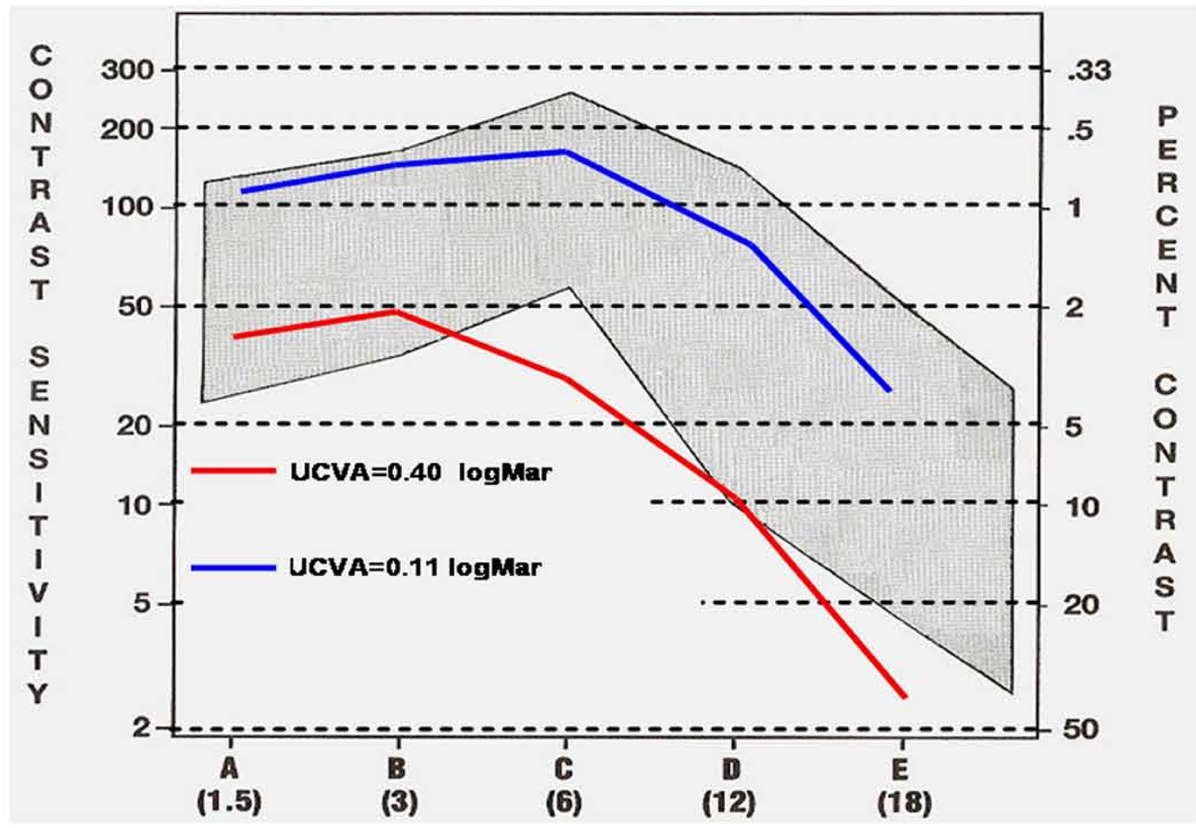
Results

Mean Baseline LogMAR UAVA was 0.40 improving to 0.107 at the end of the treatment, approximating 3 lines of improvement in acuity. 78% of this improvement was maintained after 6 months, 76% was maintained after 12 months and 74% was maintained after 24 months. Mean baseline UCSF at 1.5, 3, 6, 12, 18 cpd was: 39, 41, 23, 7, 2 improving to: 117, 145, 148, 61, 18. Average 82% of this improvement was maintained after 6 months, 79% was maintained for 12 months and 75% was maintained for 24 months. Mean refractive error in all groups remained unchanged.

Table 1. Summary of no. of lines of LogMAR improvement, Percentage and no. of eyes treated

	Unaided VA improvement (LogMAR ± SD)	Percentage of the improvement maintained	Number of eyes
Immediate post-treatment	0.292 ± 0.13	N/A	244
6 month Follow up (compared to immediate post-treatment)	0.235 ± 0.12	78%	136
12 month Follow up (compared to immediate post-treatment)	0.236 ± 0.14	76%	54
24 month Follow up (compared to immediate post-treatment)	0.204 ± 0.12	74%	36

Figure 1. Improvement of Immediate post treatment on unaided Contrast Sensitivity Functions



Conclusions:

Results suggest that NVC treatment improves UAVA and UCSF in low myopes. This improvement appears to be retained for 24 months after treatment.

Graph 1. Unaided VA is retained for 24 months after treatment

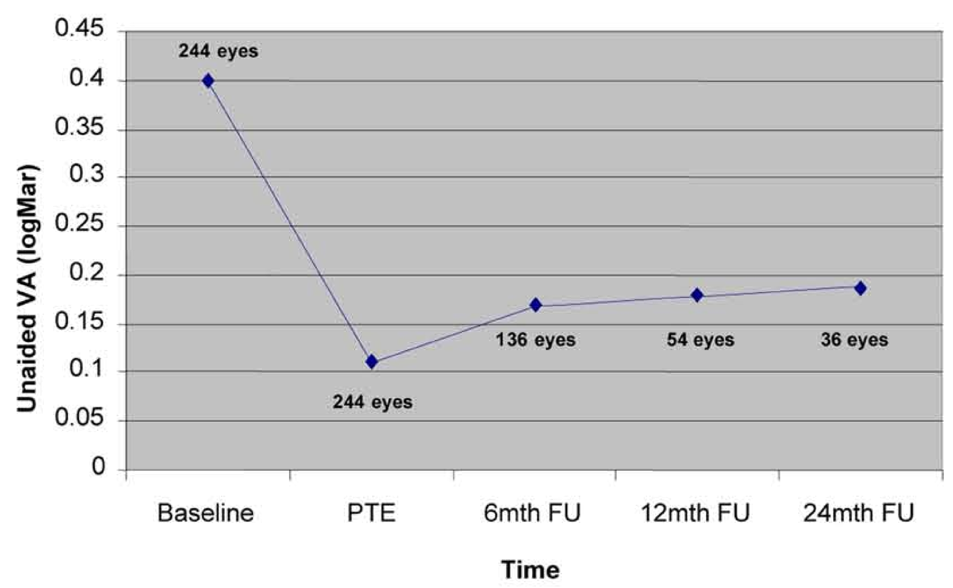
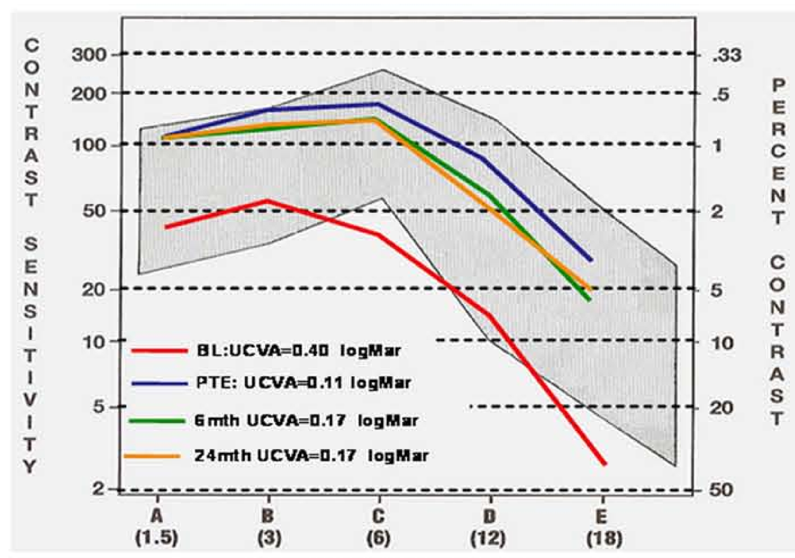


Figure 2. Unaided Contrast Sensitivity Function is retained for 24 months after treatment



References

1. Hubel, D. H. & Wiesel, T. N. Receptive fields, binocular interaction and functional architecture in the cat's visual cortex. *J. Physiol. (Lond.)* **160**, 106-154 (1962).
2. Polat, U. Functional architecture of long-range perceptual interactions. *Spat Vis* **12**, 143-62 (1999).
3. Geisler, W. S. & Albrecht, D. G. Visual cortex neurons in monkeys and cats: detection, discrimination, and identification. *Vis Neurosci* **14**, 897-919 (1997).
4. Kasamatsu, T., Polat, U., Pettet, M. W. & Norcia, A. M. Colinear facilitation promotes reliability of single-cell responses in cat striate cortex. *Exp Brain Res* **138**, 163-72. (2001).
5. Polat, U., Mizobe, K., Pettet, M. W., Kasamatsu, T. & Norcia, A. M. Collinear stimuli regulate visual responses depending on cell's contrast threshold. *Nature* **391**, 580-4 (1998).
6. Polat, U. & Sagi, D. Spatial interactions in human vision: from near to far via experience- dependent cascades of connections. *Proc Natl Acad Sci U S A* **91**, 1206-9 (1994).
7. Polat, U. & Sagi, D. Lateral interactions between spatial channels: suppression and facilitation revealed by lateral masking experiments. *Vision Res* **33**, 993-9 (1993).
8. Polat, U. & Sagi, D. The architecture of perceptual spatial interactions. *Vision Res* **34**, 73-8 (1994).
9. Dosher, B. A. & Lu, Z. L. Perceptual learning reflects external noise filtering and internal noise reduction through channel reweighting. *Proc Natl Acad Sci U S A* **95**, 13988-93. (1998).
10. Dosher, B. A. & Lu, Z. L. Mechanisms of perceptual learning. *Vision Res* **39**, 3197-221. (1999).
11. Sagi, D. & Tanne, D. Perceptual learning: learning to see. *Curr Opin Neurobiol* **4**, 195-9 (1994).
12. Gilbert, C. D. Adult Cortical Dynamics. *Physiological Reviews* **78**, 467-485 (1998).
13. Polat, U. & Sagi, D. in *Maturational Windows and Adult Cortical Plasticity* (eds. Julesz, B. & Kovâcs, I.) 1-15 (Addison-Wesley, 1995).
14. Polat, U., Ma-Naim, T. Belkin, M. Sagi, D. Improving vision in adult amblyopia by perceptual learning. PNAS 101, 6692-97 (2004).

Poster #54

Institute for Eye Research

PARENTAL HISTORY OF MYOPIA IN CHINESE MYOPIC CHILDREN

Vision CRC

Percy Lazon de la Jara[1,2], Les Donovan[1,2], Padmaja R. Sankaridurg[1,2], Thomas Naduvilath[2], Aldo Martinez[1,2], Arthur Ho[1,2], Xiang Chen[2,3], Julia Chen[3], Jian Ge[3], Brien Holden[1,2]

1 Institute for Eye Research, Sydney Australia; 2 Vision CRC, Sydney, Australia and 3 Zhongshan Opthalmic Centre, Guanzhou, China

PURPOSE

To assess the relationship between parental myopia, the refractive state and ocular biometry of Chinese myopic children.

METHODS

- 210 myopic children (mean age of 11 ± 2.3 years, range 6-16 years) were recruited for a longitudinal myopia progression study at the Zhongshan Ophthalmic Centre, Guangzhou, China.
- At baseline, refractive error and axial length were determined on cyclopleged eyes using an open field auto-refractor (NVision-K 5001, Shin Nippon, Japan) and an interferometer (IOLMaster, Carl Zeiss Meditec, Germany).
- Data on parental myopia was collected using a survey completed by parents.

STATISTICAL ANALYSIS

- Data from the two eyes were averaged prior to data analysis.
- Statistical association of spherical equivalent (SE) and axial length (AL) with parental history of myopia was investigated using correlations and linear mixed models.

RESULTS

- Of the 210 myopic children, 40 had two myopic parents (19%), 90 had one myopic parent (43%) and 80 had no myopic parents (38%).
- At baseline, the mean SE was -1.88 ± 0.64D (range -0.75 to -3.75D) and the mean AL was 24.5±0.7mm (range 23.0 to 27.8mm)

Figure 1. Baseline cycloplegic refraction based on the average spherical equivalent of two eyes.

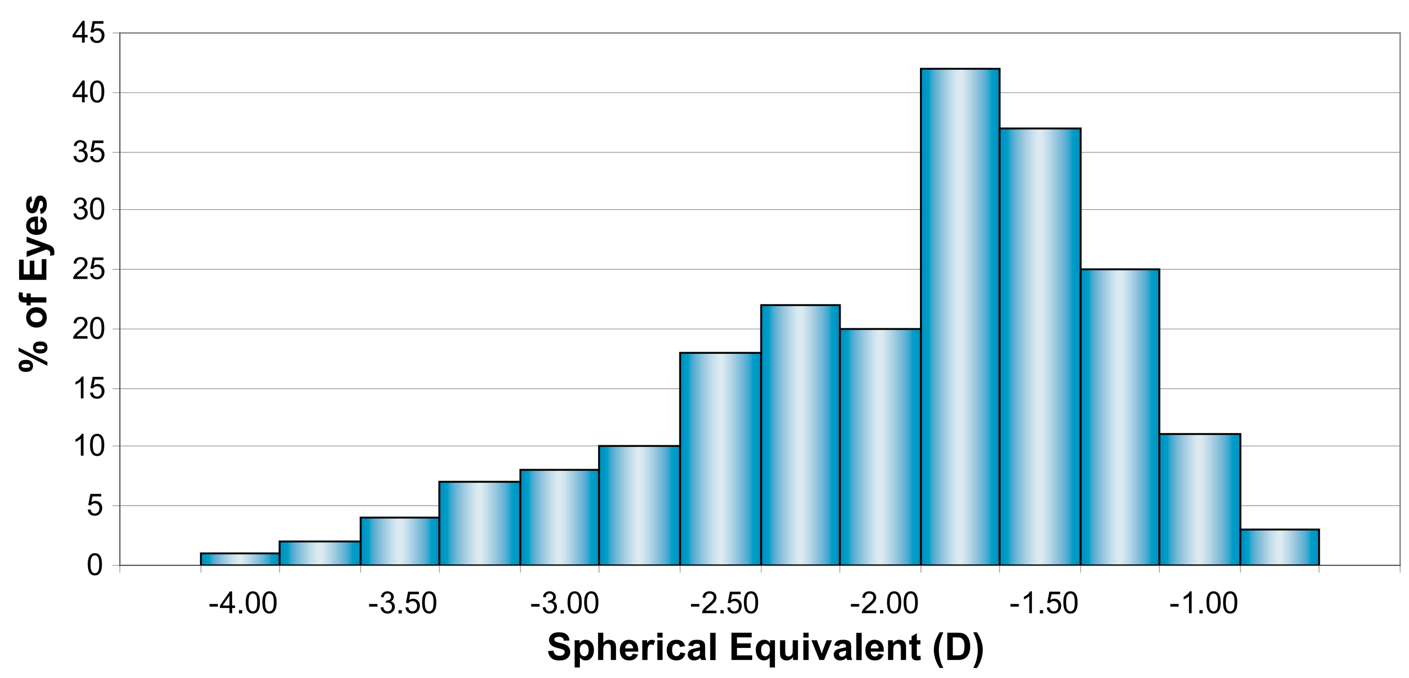
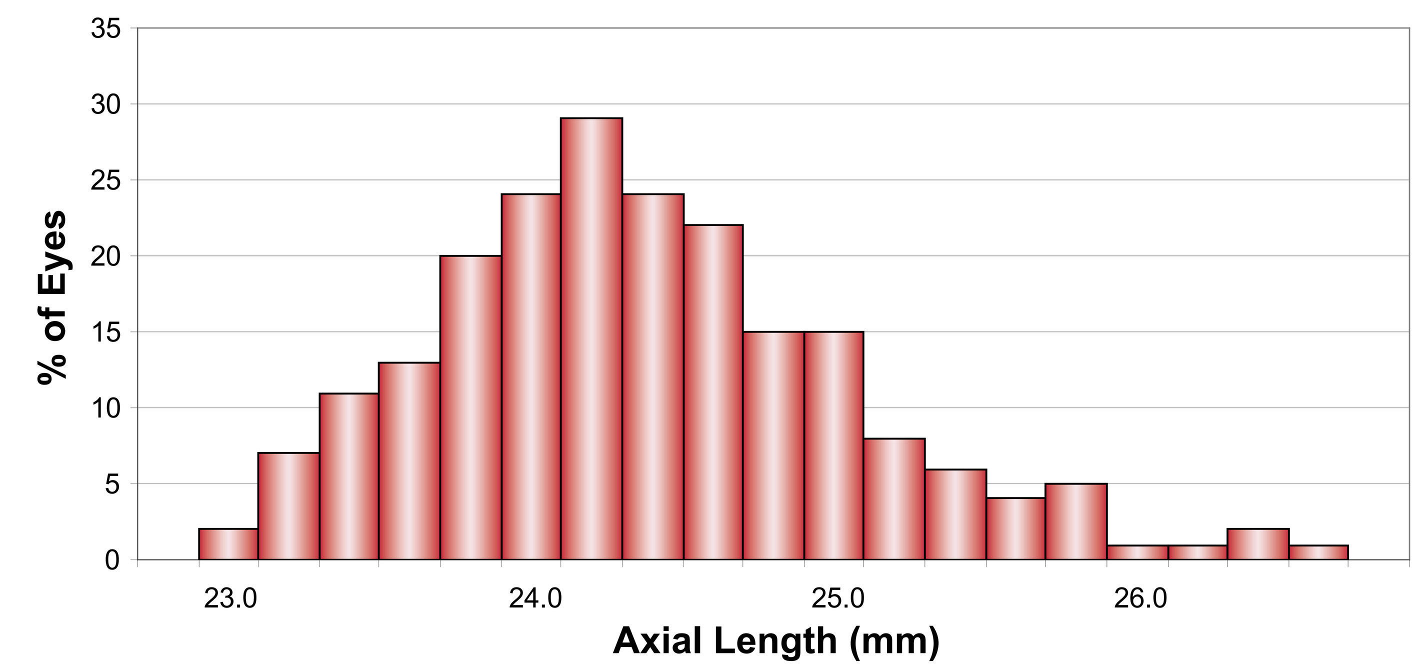


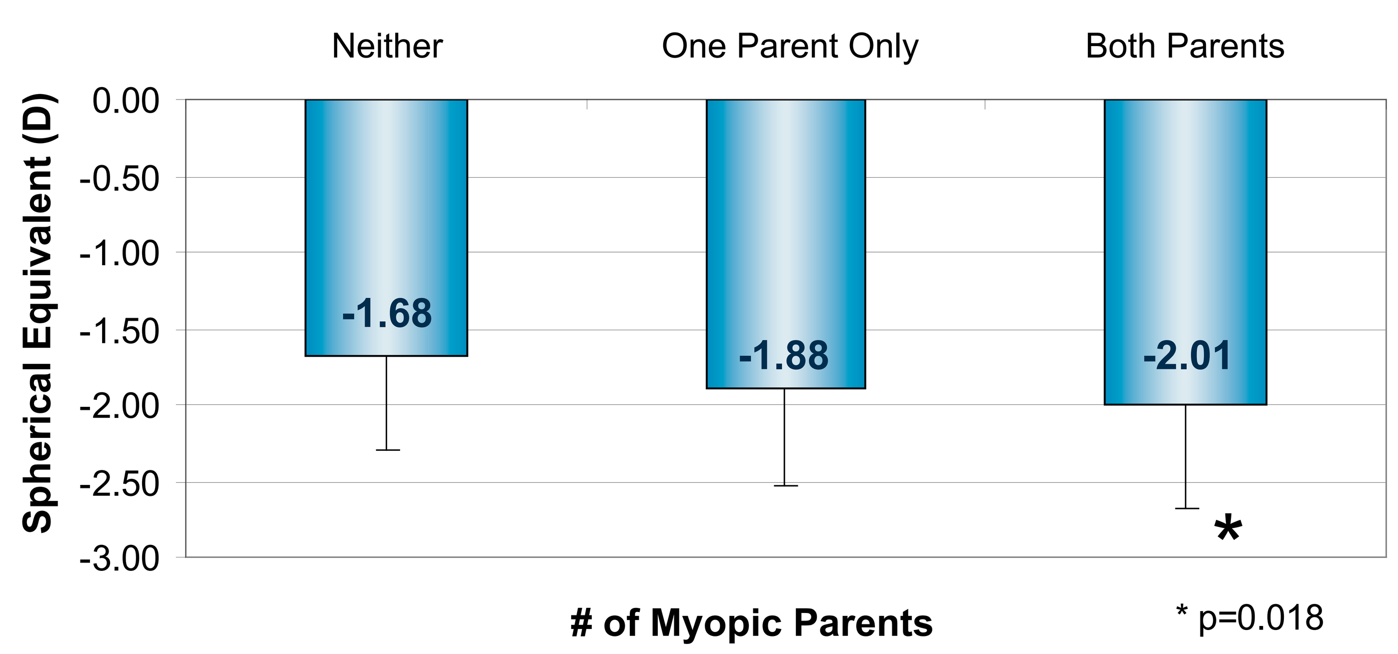
Figure 2. Baseline axial length based on the average of two eyes.



SPHERICAL EQUIVALENT AND PARENTAL MYOPIA

There was an association between SE and parental myopia ($p<0.05$). Children with two myopic parents had greater myopia compared to those with no myopic parents ($p=0.018$).

Figure 3. Parental myopia and level of myopia in their offspring.

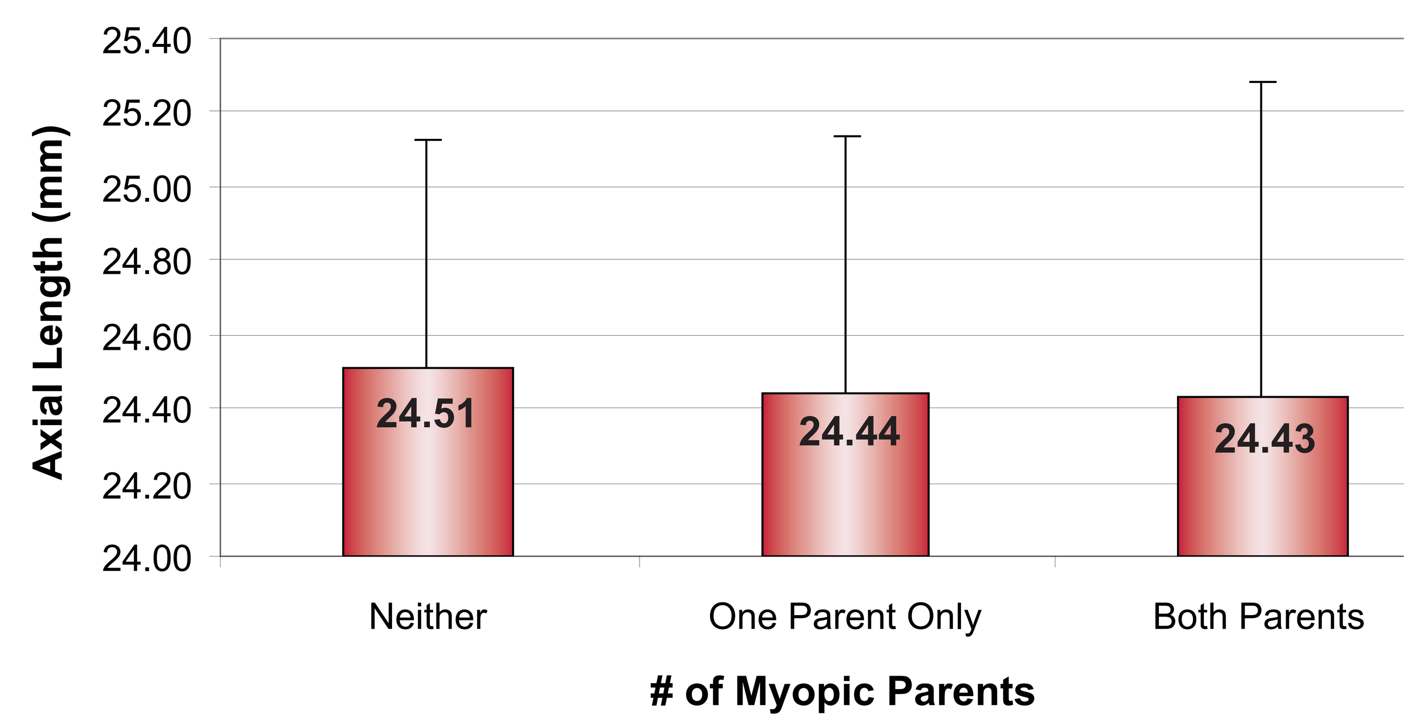


The multivariate analysis, after adjusting for gender, years of spectacle usage, hours per week reading books and baseline AL, showed that the mean spherical equivalent increased by -0.15D per myopic parent ($p=0.007$).

AXIAL LENGTH AND PARENTAL MYOPIA

Interestingly, there was no association between parental myopia and AL.

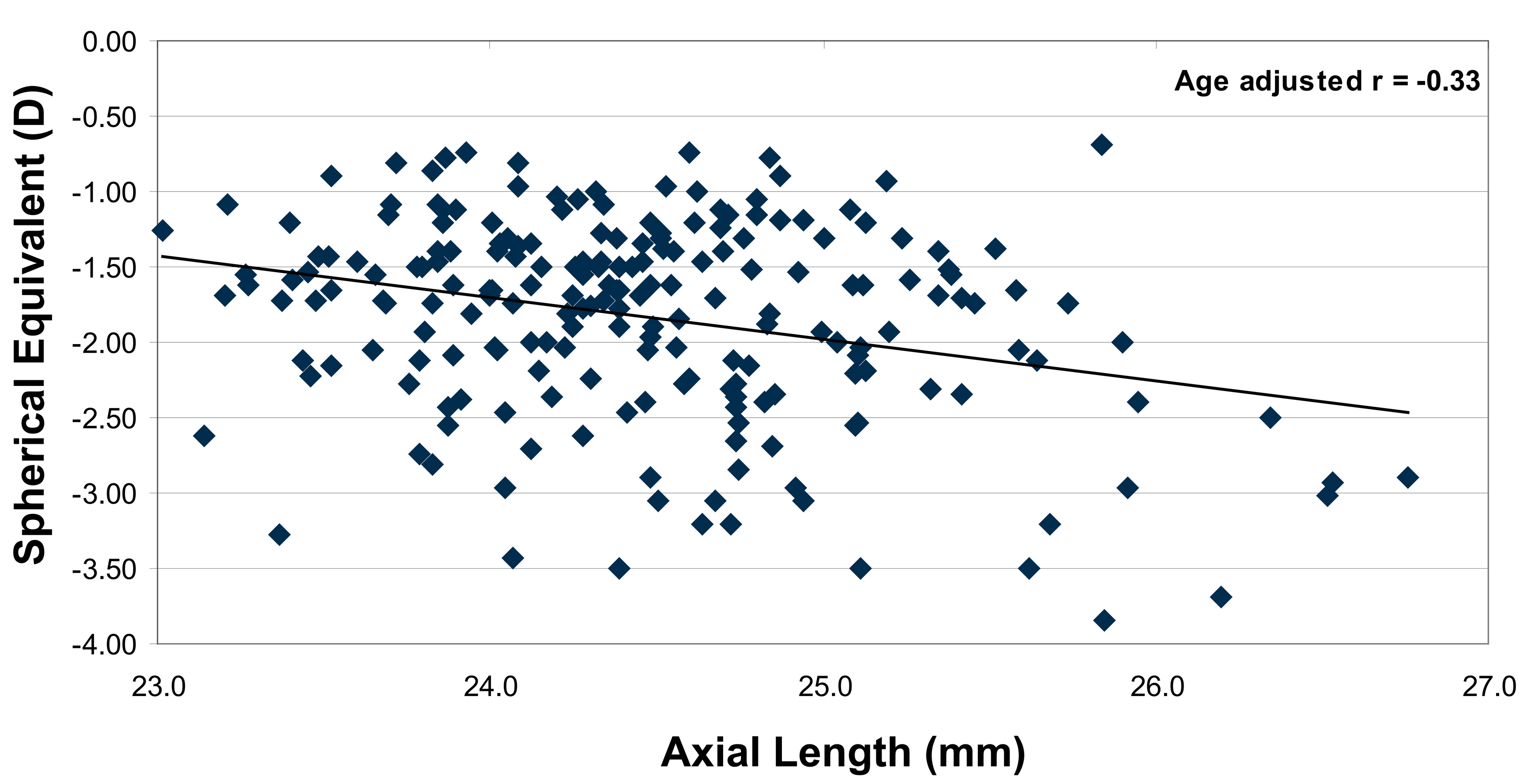
Figure 4. Parental myopia and AL on their offspring



SPHERICAL EQUIVALENT AND AXIAL LENGTH

When SE and AL were considered, it appears that there was only a weak correlation with AL after adjustment for age ($r=-0.33$, $p<0.001$)

Figure 5. Pearson correlation between SE and AL.



CONCLUSION

- Similar to previous studies reporting an association of myopia in children with parental myopia [1-3], spherical equivalent refractive error of children with two myopic parents was more myopic than those with one or no myopic parent.
- In contrast to previous reports [2], we did not find an association of axial length and parental myopia. The mean axial length of children with two or one myopic parent was shorter than myopic children with no myopic parents. Similar results have been reported in pre-myopic Chinese children [4].
- The weak correlation between spherical equivalent and axial length suggests that factors other than axial length (i.e. the crystalline lens [5-7]) could be contributing to this variance in spherical equivalent refractive power and needs to be explored further.

REFERENCES

1. *Hirsch, M.J. and D.L. Ditmars, Refraction of young myopes and their parents--a reanalysis. Am J Optom Arch Am Acad Optom, 1969. 46(1): p. 30-2.*
2. *Zadnik, K., et al., The effect of parental history of myopia on children's eye size. Jama, 1994. 271(17): p. 1323-7.*
3. *Gwiazda, J., et al., Emmetropization and the progression of manifest refraction in children followed from infancy to puberty. Clin Vis Sci, 1993(8): p. 337-44.*
4. *Lam, D.S., et al., The effect of parental history of myopia on children's eye size and growth: results of a longitudinal study. Invest Ophthalmol Vis Sci, 2008. 49(3): p. 873-6.*
5. *Mutti, D.O., et al., Optical and structural development of the crystalline lens in childhood. Invest Ophthalmol Vis Sci, 1998. 39(1): p. 120-33.*
6. *Zadnik, K., et al., Ocular component data in schoolchildren as a function of age and gender. Optom Vis Sci, 2003. 80(3): p. 226-36.*
7. *Zadnik, K., et al., Longitudinal evidence of crystalline lens thinning in children. Invest Ophthalmol Vis Sci, 1995. 36(8): p. 1581-7.*

DISCLOSURE - none