

ACCOMMODATIVE MICROFLUCTUATIONS ARE NOT RELATED TO EYE SIZE

Poster #12



GLASGOW
CALEDONIAN
UNIVERSITY

Dirk Seidel, Lyle S Gray and Niall C Strang

Glasgow Caledonian University, Glasgow, Scotland, UK

INTRODUCTION

Previous studies have shown increased accommodative microfluctuations in myopes compared to emmetropes. However, variability within the myopic groups has been evident with some individuals or subgroups having fluctuations similar to those of emmetropic eyes (Figure 1).

It could be speculated that posterior chamber enlargement in myopic eyes creates additional circumferential space allowing increased freedom of movement of the crystalline lens which may result in increased accommodative microfluctuations.

This study investigates the relationship between eye size and the microfluctuations of accommodation.

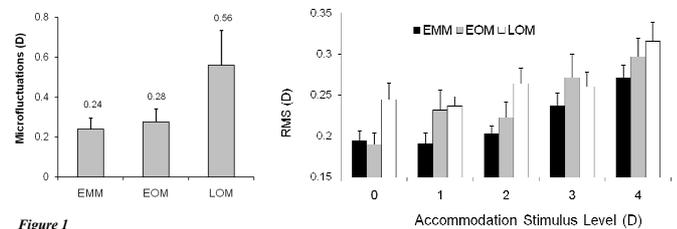


Figure 1

Increased microfluctuations shown by late-onset myopes (LOM) compared to emmetropes (EMM) and early-onset myopes (EOM). Subjects viewed high contrast Badal targets at a vergence of -4.0 D (left) and vergence levels between 0 and -4.0 D (right). Data from Seidel et al (2003) and Day et al (2006)

METHODS

15 subjects with refractive errors (MSE) ranging from -7.00D to + 4.00D and axial lengths ranging from 21.3mm to 27.2mm participated with informed consent in the study. All subjects had normal ocular health and VA of 0.0 logMAR or better. Subjects viewed a high contrast Maltese cross target in a 12D Badal lens system, monocularly at dioptric vergences of 0.0D and 4.5D. Refractive correction was achieved by adjusting the Badal lens. Microfluctuations of accommodation were recorded with a modified Shin Nippon SRW-5000 optometer for a period of 2 minutes and biometric measures of axial length and anterior chamber depth were obtained using the Zeiss IOL master (Figure 2).

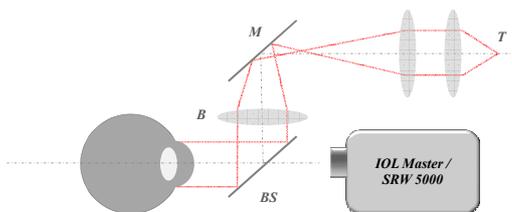


Figure 2

Experimental set up. Subjects viewed an 80% contrast Maltese cross (T) in photopic conditions via a Badal lens (B), beam splitter (BS) and plane mirror (M).

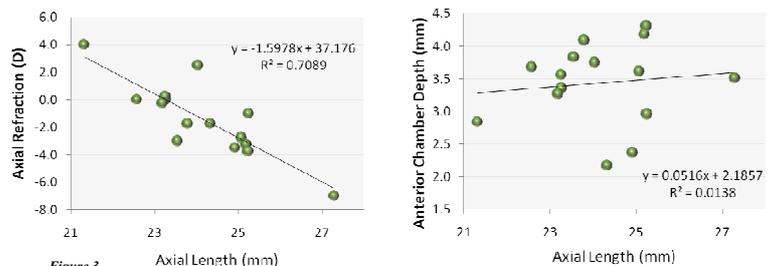


Figure 3

Refractive error (left) and anterior chamber depth (right) plotted against axial length for all subjects.

RESULTS

The magnitude of the accommodative microfluctuations increased significantly ($p=0.002$) and anterior chamber depth (ACD) decreased significantly ($p=0.002$) when the near target was viewed. Axial length increased slightly with increasing target vergence ($p=0.043$) (Figure 4).

There was a significant ($R^2=0.74$; $p<0.001$) negative correlation between the increase in the magnitude of the fluctuations for the 4.5D target and the magnitude found when viewing the 0.0D target (Figure 5 C).

The magnitude of the accommodative microfluctuations was not significantly correlated with axial length or anterior chamber depth.

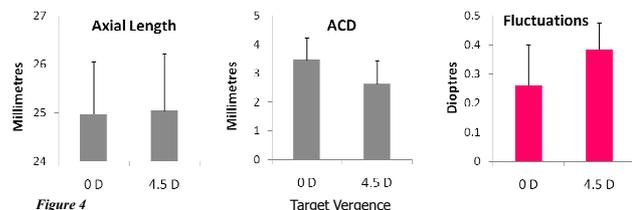


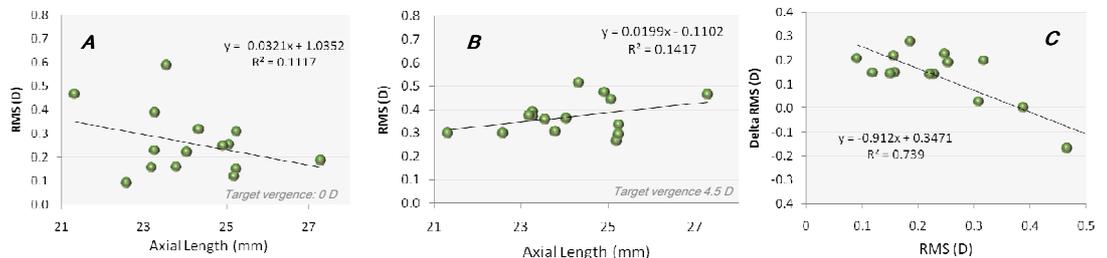
Figure 4

Axial length, anterior chamber depth (ACD) and the magnitude of the accommodative microfluctuations for the vergence levels. Error bars represent one standard deviation.

Figure 5

The root mean square (RMS) of the accommodative microfluctuations is not related to axial length for 0 D target vergence (A) and 4.5 D target vergence (B).

The relative change in the microfluctuations with increasing vergence demand is negatively correlated with the baseline fluctuations for 0.0 D target vergence (C).



CONCLUSIONS

1. Accommodation microfluctuations are unrelated to eye size.
2. This suggests that accommodation microfluctuations are not the result of plant noise within the accommodation system.
3. Accommodation microfluctuations therefore have the potential to provide negative feedback signals to the accommodation response controller.

REFERENCES

Day, M., N. C. Strang, D. Seidel, L. S. Gray and E. A. Mallen (2006). "Refractive group differences in accommodation microfluctuations with changing accommodation stimulus." *Ophthalmic Physiol Opt* 26(1): 88-96.
Seidel, D., L. S. Gray and G. Heron (2003). "Retinotopic accommodation responses in myopia." *Invest Ophthalmol Vis Sci* 44(3): 1035-41.

Effect of target spatial frequency on accommodative responses of emmetropes and myopes

Poster #13

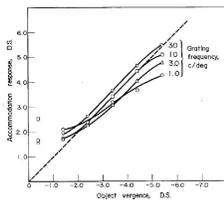
W. Neil Charman, John Taylor, Clare O'Donnell, Hema Radhakrishnan
Faculty of Life Sciences, University of Manchester, United Kingdom

Introduction

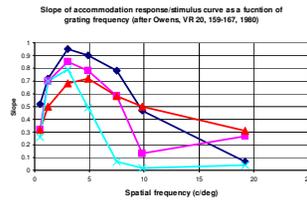
It has been suggested that:

- Myopes have a lower accommodation response/stimulus gradient, particularly monocularly when negative lenses are used to vary the stimulus. (McBrien & Millodot, 1986; Gwiazda et al., 1993,1995; Drobe & St Andre 1995; Abbott et al., 1998)
- Myopes have a reduced sensitivity to defocus blur. (Jiang, 1997; Rosenfield and Abraham-Cohen, 1999; Collins et al., 2006)
- Hyperopic defocus due to accommodation lag and/or aberration blur leads to axial elongation and myopia.

Does this mean that myopes make less use of information at higher spatial frequencies, since these are more sensitive to defocus? Previous studies using sine grating targets (not differentiated by refractive group) show two alternative types of behaviour the difference perhaps being due to the effect of instruction: (Charman & Tucker, 1997; Owens, 1980; Ciuffreda & Hokoda, 1985)



“Fine focus” control?
(Charman & Tucker, 1977)



“Contrast” control
(Owens, 1980)

Purpose

To compare the response/stimulus curves of emmetropes and myopes for 1) targets containing only information at high spatial frequencies and 2) sinusoidal gratings.

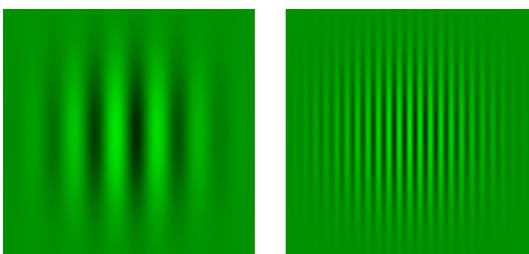
Methods

Subjects:

- 10 emmetropes (-0.50<MSE<1.50 D, mean MSE +0.19 D).
- 10 myopes (-6.75<MSE<-1.00 D, mean MSE - 2.89 D, corrected with soft CL, mean age 25.75 yrs). Myopic group included early-onset (7) and late-onset (3) myopes.

Targets and instrumentation:

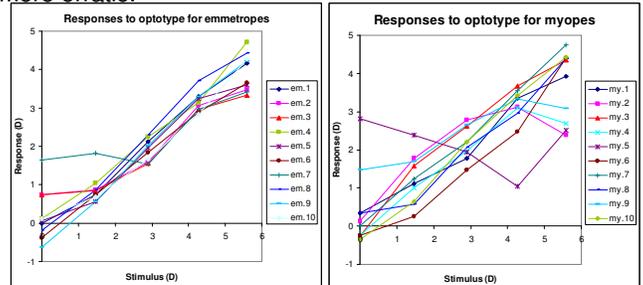
- Grating frequencies 1,4,8 and 16 c/deg, 6/30 optotype (6 deg field Gabors, 45 cd/m², green, 80% contrast, dark surround).
- Targets at 1 m, accommodative demand varied with negative lenses (nominal stimulus range 0 to 6.0 D).
- Monocular RE responses measured with a Shin-Nippon SRW-500 autorefractor (LE occluded).



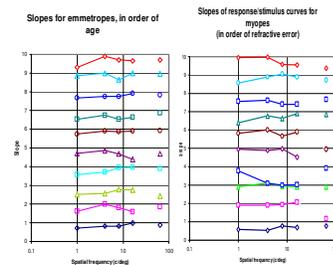
Example of 1 c/deg and 4 c/deg gratings. The boundaries were masked with a near aperture.

Results

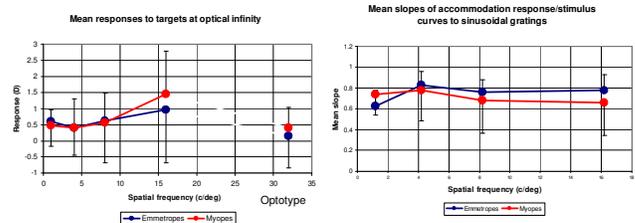
The response/stimulus curves for the 6/30 optotype are shown. The mean slopes were: Em 0.806+/-0.154 vs. My 0.661+/-0.315 (p= NS). The myopes' responses were perhaps more erratic:



Inspection of the slopes appears to suggest a mixture of “fine focus” and “contrast” behaviour for both groups:



Most subjects found it hard to relax accommodation when viewing the 16 c/deg grating at optical infinity (i.e. target at 1 m through -1D lens) and there was little difference between the mean data for the emmetropes and myopes:



Accommodative error indices (which express mean lag) showed that two myopes had poor results for particular targets. Measurements repeated after further training and encouragement on these poorly responding myopes improved the accommodative response for these targets.

Conclusions

- The data do not support the suggestion that, on average, myopes have more difficulty than emmetropes in accommodating to high frequency targets.
- In both refractive groups some subjects responded poorly to particular targets.
- Poor responses might be due to inter-subject variations in the reliance placed on particular components of accommodation or cues (e.g. blur, proximity, binocular, tonic, voluntary, colour).
- It may be that different myopic groups (e.g. all younger, progressing) would have shown differences.
- In our small sample, there was no evidence that EOM, LOM, progressing or non-progressing myopes were associated with different accommodative behaviours.



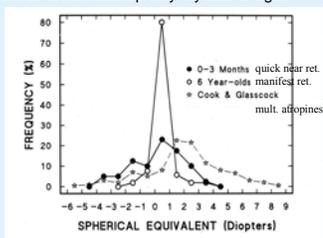
Cycloplegic and Noncycloplegic Refractions of Chinese Neonates

Chen Jie¹ Xie Ailan¹ Hou Lijie¹ Su Yanfeng¹ Frank Thorn^{1,2}

¹Wenzhou Medical College, Wenzhou, China; ²New England College of Optometry, Boston, USA

Introduction

Western infants tend to be hyperopic with great refractive variability when examined with cycloplegic retinoscopy. Cook and Glascock (1952) showed a mean spherical equivalent (SE) equivalent of +2D during the first month of life while others have found a mean SE of +1D to +2D at slightly older ages in infancy. Results from noncycloplegic near retinoscopy vary between studies showing 1.0D to 2.0D less plus than cycloplegic studies (Thorn et al, 1996). Infants eyes then emmetropize so almost all are emmetropic by 6 years of age.



There are few refractive studies of Chinese infants and few that compare cycloplegic and noncycloplegic refractions. Thus, it is important to find the neonatal refractive starting point in a population at high risk for myopia. This is the start of a longitudinal study projected to last through infancy.

Purpose

To examine neonatal Chinese infants with both cycloplegic and noncycloplegic retinoscopy to describe and compare the distribution of refractive errors for both techniques in these infants.

Methods

Subjects

185 infants between 1 and 6 days of age who were born at full term. All were healthy and at birth and had normal deliveries.

81 of these were also examined under cycloplegia.

Procedure

Retinoscopy was performed by two experienced pediatric ophthalmologists (CJ & HL) in the obstetrics department of the Wenzhou Medical College Second Affiliated Hospital. Parents signed informed consent forms after being carefully informed about the procedures. The Tenets of Helsinki were carefully adhered to.

Subjects

were the babies available when the clinicians came to the hospital and whose parents agreed to the procedures.

Noncycloplegic retinoscopy (NRx) was performed in a dark room using Mohindra's near retinoscopy technique as described by Thorn (1996).

Cycloplegic retinoscopy (CRx) was performed after NRx with two drops of a 2.5% phenylephrine+0.5% cyclopentolate mixture.

Basic Results

Refractive Distributions

NRx SE distribution: mean = +0.58D±2.32D.

CRx SE distribution: mean = +3.55D±2.39D.

(NRx SE subgroup: mean = +0.38D±2.99D.)

This does not differ from the NRx of the whole sample.

Neither distribution differs significantly from normality.

CRx vs NRx

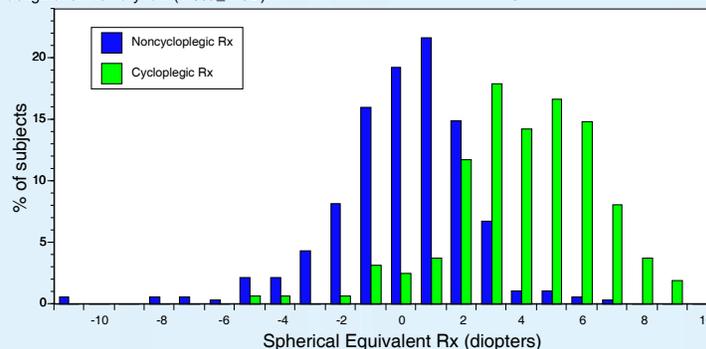
Correlation between CRx and NRx SE is modest:

Examiner 1: r = 0.76 OD, 0.73 OS

Examiner 2: r = 0.72 OD, 0.70 OS

Bland-Altman analysis shows CRx SE – NRx SE is independent of SE.

Prevalence of astigmatism is very low (1.6%±1.0D).



Discussion

For slightly older infants in the West, less hyperopia and higher amounts of astigmatism are risk factors for the later development of myopia. The Chinese neonates have relatively high amounts of hyperopia under cycloplegia and little astigmatism. Yet they are at risk to become myopic earlier and to a greater degree than Western children.

Is this because the Chinese infants are so young and a similar study performed on neonates in the West would show similar results? OR

Are refractive risk factors in Chinese children different than those in the West suggesting different mechanisms?

We are collecting refractive data from some of these infants at about 6 months of age and these data will help resolve this question.

The difference between CRx and NRx in our neonates is much greater than that shown in infants and children in previous studies. The Mohindra correction of 0.75D accounts for little of this difference. This suggests that Chinese neonates have strong tonic accommodation that may differ from Western neonates OR may relax as the infants' hyperopia emmetropizes.

The Rx of Chinese neonates and of infants in Boston (Gwiazda et al) is uncorrelated with parental Rx. This shows that the strong relationship between parental and teenage refraction is based on mechanisms that occur well after birth.

Other Results

Reliability Correlations

Both NRx and CRx SEs are highly correlated between examiners although CJ finds slightly more plus (+0.16D):

NRx: r = 0.94 OD, 0.93 OS; CRx: r = 0.96 OD, 0.97 OS

& Highly correlated between eyes:

NRx: Examiner 1, r = 0.95; Examiner 2: r = 0.97

CRx: Examiner 1, r = 0.94; Examiner 2, r = 0.95

Risk Factor Correlations

Correlation between neonatal SE and various risk factors are very low. For example:

CRx vs birth weight: r = 0.03 ns

NRx vs parental SE: r = -0.08 ns

CRx vs parental SE: r = 0.09 ns

Conclusions

1. Chinese neonates have more hyperopia under cycloplegia and less astigmatism than infants in Western studies. Yet they are at high risk for myopia.
2. Chinese neonates' noncycloplegic Rx's are about 3 diopters less hyperopic than their cycloplegic Rx's indicating high amounts of tonic accommodation.
3. 6 month follow-up data will determine if these differences between East and West exist because neonates differ from older infants OR because Chinese and Western infants differ from each other.

Acknowledgements

This project was supported by Zhejiang Nature & Science Research Foundation (ZJNS602168, 2004BA720A16).

We thank Tom Norton for suggesting this project and the staff of the obstetrics department at the Wenzhou Medical College Second Affiliated Hospital for their assistance.

Expression of Adenosine Receptors in Form-Deprivation Myopia of Guinea Pigs.

Dongmei Cui¹, Klaus Trier², Junwen Zeng¹, Jianmin Hu¹, Xiao Yang¹, Jian Ge¹.

State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, SunYat-sen University, China¹.

Trier Research Laboratories, Tingskiftevej 6, DK-2900 Hellerup, Denmark².

Corresponding author: Jian Ge, e-mail: gejian@mail.sysu.edu.cn

Aims: Systemic treatment with adenosine receptor antagonists 7-methylxanthine has been reported to affect the biochemistry and ultrastructure of rabbit sclera. This study was conducted in order to determine whether adenosine receptors (ADORs) are present in human scleral fibroblasts (HSF), retinal pigment epithelium (RPE) and their protein expression changes in form deprivation myopia (FDM) of guinea pigs.

Methods: HSF and RPE were cultured in vitro. Confocal fluorescence microscopy was used to study the distribution of ADORs in the HSF and RPE. Three-week old Guinea pigs were monocularly deprived using a diffuser. Twenty-one days after the induction of FDM, the retina, choroids and sclera were collected. Confocal fluorescence microscopy and western blotting analysis were used to detect the changes of ADORs expression. Levels of ADORs protein expression were statistically compared between FDM and control eyes.

Results: ADORs were expressed in both HSF and RPE, but their cell distribution was different. Twenty-one days after the induction of myopia, ADORA1 was observed statistically decreases in protein expression but ADORA2B was increased in the posterior sclera of FDM-affected eyes ($p < 0.05$ vs. control eyes). ADORA2A and ADORA3 had no significant changes in the posterior sclera.

Conclusion: All four subtypes of ADOR were found in HSF and RPE. Different distribution and expression of ADOR may play different roles in FDM of guinea pigs.

This study was supported by grant 2007CB512200 from the National Key Basic Research Program, China and a grant from Bagenkop Nielsens Myopia-Foundation, Denmark.

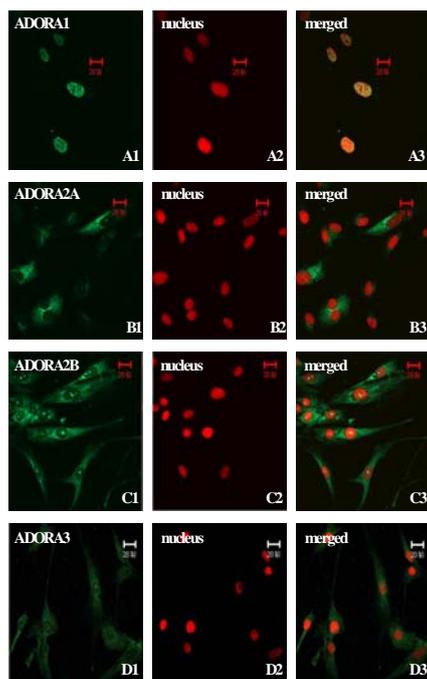


Fig.1. Distribution of ADORA1, ADORA2A, ADORA2B, and ADORA3 in HSF in vitro using indirect immunofluorescence (400×). Secondary antibody is marked by FITC (green) and nucleus dyed by PI (red). Third vertical row shows the combined images.

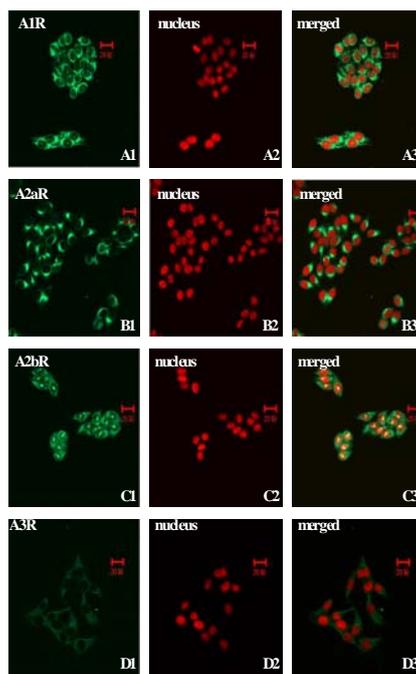


Fig.2. Distribution of ADORA1, ADORA2A, ADORA2B, and ADORA3 in RPE in vitro using indirect immunofluorescence (400×). Secondary antibody is marked by FITC (green) and nucleus dyed by PI (red). Third vertical row shows the combined images.

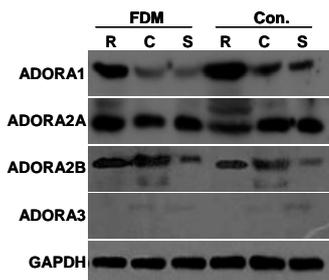


Fig.3. Western blotting analysis verifies expression of ADOR protein in the retina, the choroids and the sclera of FDM guinea pigs.

Table 1. Changes of ADOR subtypes expression in guinea pigs (FDM/Con.)

	RETINA	CHORIODS	SCLERA
ADORA1	74.5±8.1	78.4±7.2	77.5±6.5
ADORA2A	126.9±21.9	105.3±10.2	108.5±9.0
ADORA2B	166.7±30.6	145.5±8.8	118.7±13.2

TEMPORAL PROPERTIES OF REPEATED HYPEROPIC DEFOCUS IN THE GUINEA PIG EYE

Poster #32



Amelia J. Leotta and Sally A. McFadden

School of Psychology, The University of Newcastle, NSW 2308



INTRODUCTION

In all species studied including humans, when a growing eye wears a spectacle lens it will adjust its growth rate and change its refractive error to compensate for any imposed defocus.

Spectacle lens compensation (SLC) has been shown in many species, including chicks¹, tree shrews², marmosets³, guinea pigs⁴ and monkeys⁵.

While the temporal properties of such spectacle lens compensation have been investigated in the chick^{6,7}, there have only been preliminary investigations in the mammalian eye. The data from the chick suggests that the signal that leads to ocular elongation arising from hyperopic blur decays within 30 minutes⁷.

Our aim was to investigate the temporal properties of hyperopic defocus in the guinea pig.

METHOD

42 guinea pigs wore -4D lenses on their right eye for repeated 15 minute periods with varying dark intervals in between these episodes of visual experience (Fig. 1).

Ocular Measurements: At 18 days of age, refractive error (using streak retinoscopy), corneal curvature (using infrared videoretinoscopy, Fig. 2) and ocular structures (using high frequency ultrasound, Fig. 3) were measured under isoflurane anaesthesia.

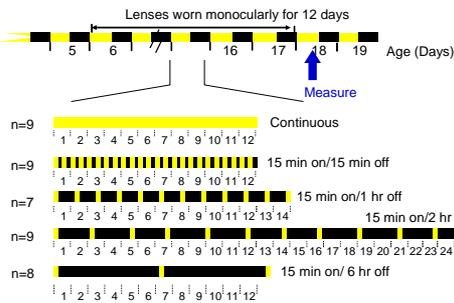


Figure 1. Light cycles for guinea pigs wearing -4D lenses

OCULAR MEASUREMENTS

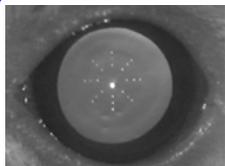


Figure 2. Example image from infrared keratometry.

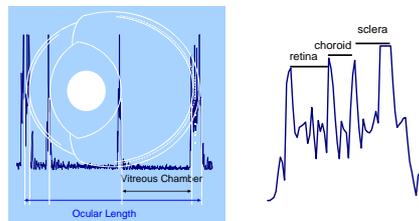


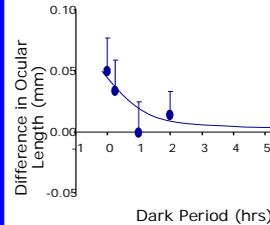
Figure 3. A-scan ultrasound of guinea pig eye

RESULTS

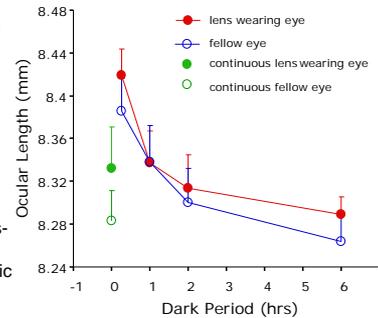
FREQUENCY EFFECT

As the frequency of the light periods increased, both the lens-wearing and the non-lens-fellow eye became more elongated (A) and more myopic (B).

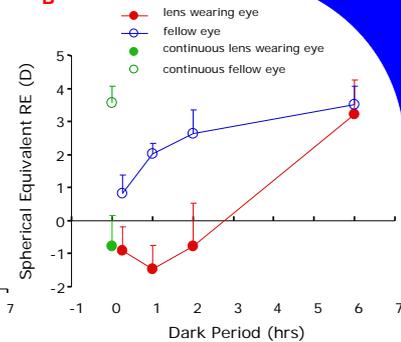
C



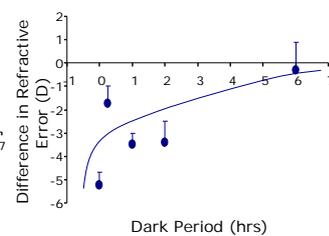
A



B



D



DECAY OF HYPEROPIC DEFOCUS

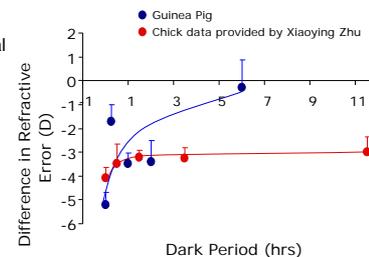
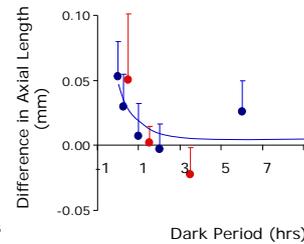
Guinea pigs who wore -4D lenses continually became most myopic ($M = 4.3D$). As the dark period increased in length, the hyperopic defocus signal decayed. The decay rate was more rapid for the ocular elongation (C) than for the refractive status of the eye (D).

Greater myopia and more robust SLC was observed with more frequent visual episodes of hyperopic defocus.

DECAY OF HYPEROPIC DEFOCUS IN THE CHICK AND THE GUINEA PIG

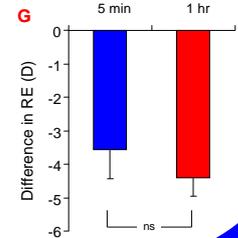
Axial elongation decays to 50% when the dark interval between episodes is approximately 30 minutes in both mammals and birds (E), suggesting that the signals that control axial elongation are phylogenetically conserved.

However, the consequences of axial elongation on refractive status varies between species (F). The myopia that results from hyperopic defocus decays much more rapidly in the mammal (50% decay at one hour) than the chick, where it appears to last several days.



RISE TIME OF HYPEROPIC DEFOCUS

Preliminary RE data shows that guinea pigs experiencing one hour dark episodes need only five minutes of light to compensate for the hyperopic defocus from -4D lenses, this being as effective as one hour of light (G). This is comparable to the short time required for chicks⁷.



CONCLUSION

- Short multiple visual exposures, regardless of blur, act as a myogenic stimulus. The more frequent the exposures, the stronger the resulting myopia.
- Only five minutes of repeated episodes of hyperopic defocus are sufficient to cause spectacle lens compensation.
- In mammals, the ocular elongation caused by a minus lens decays in 30 minutes (like the chick), but the resulting myopia is more resilient and does not decay until at least an hour has passed between episodes.
- This implies that frequent exposures to blur with short periods in between will lead to myopia in humans

REFERENCES

1. Schaeffel, F., & Howland, H. C. (1991). *Vis Res*, 31, 717-734.
2. Norton, T. T., Sieglwart, J. T., & Amedo, A. O. (2006). *Invest Ophthalmol & Vis Sci*, 47, 4687-4699.
3. Graham, B., & Judge, S. J. (1999). *Vis Res*, 39, 189-206.
4. McFadden, S. A., Howlett, M. H. C., & Mertz, J. R. (2004). *Vis Res*, 44, 643-653.
5. Hung, L.F., Crawford, M.L., & Smith, E.L. (1995). *Nat Med*, 1, 761-765.
6. Zhu, X., Liu, Y., Garniez, J., & Wallman, J. (2004). *Invest Ophthalmol & Vis Sci*, 45, [abstract] 4285.
7. Zhu, X., & Wallman, J. (2008). Personal Communication.

CONTACT DETAILS

Amelia Jane Leotta
Vision Sciences Laboratory
School of Behavioral Sciences
Ph: 49 217310
Amelia.Leotta@newcastle.edu.au



DECAY TIME OF THE SIGNAL UNDERLYING MYOPIA INTERACTS WITH LENGTH OF EXPOSURE TO HYPEROPIC DEFOCUS IN THE CHICK

Hannah E. Bowrey and Sally A. McFadden

School of Psychology, The University of Newcastle, NSW 2308

1 AIM

When hyperopic defocus is imposed on a growing eye with a negative spectacle lens, the eye becomes elongated and develops myopia, the degree of which is matched to the power of the spectacle lens so as to eliminate the imposed defocus.

The temporal properties of the myopic signal underlying such spectacle lens compensation (SLC) has been estimated by varying the length of repeated episodes of lens-wear (rise-time) or by varying the time between these episodes (decay-time).

In the chick, for repeated saturated periods of wearing a -7D lens, with darkness in between the lens wearing episodes, the signal for ocular elongation decays to 50% if these dark periods are approximately 30 min¹. This suggests that the signal arising from hyperopic blur decays rapidly.

However, it has also been demonstrated that frequent repeated episodes of minus lens-wear induce greater SLC than a single period of the same total duration². In the current study, we asked whether these temporal properties may differ depending on the length of the exposure periods.

2 METHOD

Experiment 1

Chicks wore -10D or plano lenses on one eye during repeated 15 min episodes with either 15 min, 1 hr or 3 hrs of darkness between episodes. Episodes occurred during each 18 hr day period (followed by 6 hr night) and were repeated for 3 days.

Experiment 2

We compared the effect of either 15 or 30 minutes of -10D lens exposure with 1 hr of darkness between episodes.

Ocular Measurements

At the end of each experiment, refractive error (using streak retinoscopy), and ocular components (using high frequency ultrasound, Fig. 1) were measured under isoflurane.

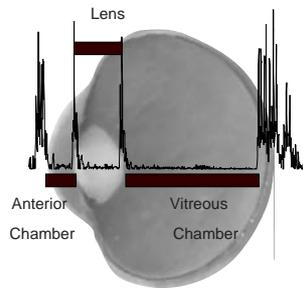


Figure 1: A-Scans used a 20 MHz transducer digitized at 100 MHz.

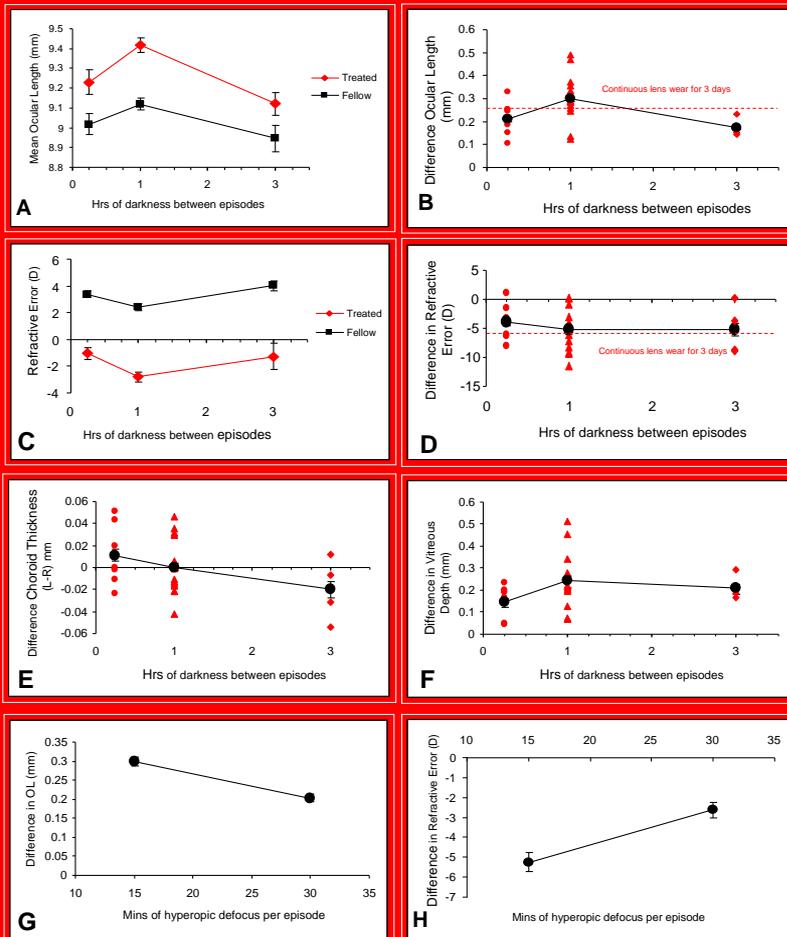


Fig. 2. A: Mean ocular length of treated and fellow eyes for 15 min, 1 h and 3 h timing conditions. B: Mean difference in ocular length for treated and fellow eyes for 15 min, 1 h and 3 h timing conditions. C: Mean refractive error of treated and fellow eye for 15 min, 1 h and 3 h timing conditions. D: Mean difference in refractive error for treated and fellow eye for 15 min, 1 h and 3 h timing conditions. E: Mean difference in choroid thickness for treated and fellow eyes for 15 min, 1 h and 3 h timing conditions. F: Mean difference in vitreous depth for treated and fellow eyes for 15 min, 1 h and 3 h timing conditions. G: Mean difference in ocular length for treated and fellow eyes in 15 min, 30 min timing condition. H: Mean difference in refractive error for treated and fellow eyes for 15 min, 30 min timing conditions.

3 RESULTS

Experiment 1

Compensation to a -10D lens was only reduced if the time of darkness between episodes was at least 3 hrs (Fig 2 A, B), a longer decay-time than previously found¹ (Fig. 3).

Experiment 2

Shorter 15 min -10D lens exposure periods were more effective in eliciting myopia over 3 days than longer 30 min periods (as measured by refractive error difference and ocular length, both $p < 0.05$, Fig. 2 G,H).

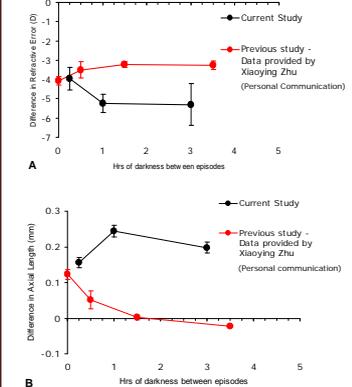


Fig. 3. A: Current study refractive error for 15 min, 1 h, 3 h timing conditions compared with previous study timing conditions (0, .5h, 1.5h, 3.5h). B: Current study axial length for 15 min, 1h, 3h conditions compared with previous study conditions (0h, 0.5h, 1.5h, 3.5h).

4 CONCLUSION

Our evidence suggests three hours of darkness between 15 min episodes of hyperopic defocus was not sufficient time for the signal to fully decay. This is a longer decay time than previously reported¹ when chicks were exposed to 30 min episodes.

We also find that in the chick eye, 15 min of brief defocus signals are more detrimental and effective in inducing myopia than longer sustained periods. This was tested by comparing 15 and 30 min off time with one hour between episodes. This effect may be due to the frequency of exposure², and not the total duration of hyperopic defocus time.

These results suggest that there is an interaction between the time of exposure to hyperopic defocus and the decay-time of the signal and suggest that the underlying signal integrator is non-linear.

REFERENCES

- Zhu X, Liu Y, Garniez J, Wallman J (2004). The Temporal Dynamics of Spectacle-Lens-Compensation in Chicks. *Invest Ophthalmol* 45, [abstract] 4285
- Winawer J, Wallman J (2002). Temporal Constraints on Lens Compensation in Chicks. *Vision Res* 42, 2651-2668

*Correspondence:

Hannah.Bowrey@newcastle.edu.au



Mathematical Modeling of Longitudinal Data for Myopia Progression



Poster #36

Frank Thorn
Myopia Research Center, New England College of Optometry, Boston, MA

Purpose

Myopia progression in schoolchildren is an orderly process that is similar in most children even though their parametric values may differ. A customized Gompertz growth function has been shown to closely fit myopia progression data in individual children in the Children's Vision Lab at the New England College of Optometry. Just as importantly this function fits the characteristics of myopia progression as we know them (Thorn et al., 2005). Other growth functions also have these characteristics (ie, Weibull, Richards, and beta functions, for a review see Yin et al., 2003) but they are more complex and do not provide useful parametric values.

In this poster I will discuss 4 concepts that must be considered when creating a mathematical model of myopia progression for individual children.

1. Almost any math model can be fit to data that does not start before the onset and extend into the offset of the myopia progression process.
2. The most dramatic and interesting features of the myopia process are its rapid onset and leisurely offset.
3. A definitive model must emerge from a full data set (usually not possible) OR must include constraints based on what we know about myopia progression.
4. A model fit to group data cannot be used to estimate a model for individual children.

Pre- & Post-Progression Fit

3. A definitive biological model must emerge from a full data set. Most longitudinal myopia progression data start after myopia progression onset and myopia onset is defined as a point well into the process (ie, SE \leq -0.5D or -0.75D). In addition, the data usually does not extend past 16 years of age.

How can we best fit such limited data? If we assume that only a least sum of squares value is necessary, we can fit anything (cosine, hyperbola, exponential, or Gompertz function) but the result may be meaningless.

Instead, we should assume that myopia progression is similar to other biological growth processes. And that myopia progression in children with limited data is similar to that in children with full data sets. This means that the limited data set must be fit with a realistic model (Gompertz function or a flexible asymmetric sigmoid function).

To do this, we put constraints on a model based on our knowledge about myopia progression. In our lab, mean emmetropia prior to myopia was +0.30D. If we place 3 data points at +0.25D during the preschool years, the function fits with a mean premyopia value of about +0.30D.

If there is no data near the asymptote of myopia stabilization, repeated curve fitting iterations often produce an asymptote with ultrahigh levels of myopia. These iterations may decrease least squares by less than 0.01%. Using a least squares value that is 1% less than its minimum value can provide approximately realistic asymptotes.

Nonsense vs Realistic Models

1. Almost any math model can fit limited data. Four models with different levels of credibility were fit to the longitudinal data of individual children for the 5 years following the first data point below -0.50D. For all 4 models, mean R > 0.95 and least squares did not differ significantly. Fits for 2 subjects are shown below as examples.

Nonsense Models:

Cosine: $Rx = R_m + (R_o/2) \cosine(ax-b)$
 Parabola: $Rx = ax^2 + bx + d$

These are nonsense models because they so obviously violate the possibilities of myopia progression. The cosine function repeatedly changes between myopia and hyperopia over a life time. The parabolic function starts and ends with ultrahigh hyperopia.

Unrealistic Model:

Exponential: $Rx = R_f + a \cdot e^{(x/c)}$

The unrealistic model starts with ultrahigh hyperopia and the offset proceeds too long before myopia stabilizes in adulthood. But it is not nonsensical like the models above.

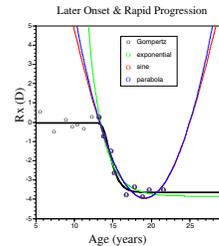
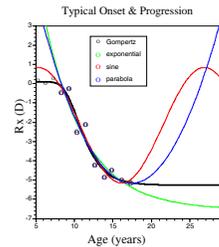
Realistic Model:

Gompertz Function: $Rx = R_o + R_f \cdot (0.07295)^{e^{(x-c)/T_o}}$

A realistic model describes a full course of refractive change from stable emmetropia in the preschool years to myopia stabilization in the late teenage years.

$y = Rx$ (spherical equivalent) at age x years.
 $R_o = Rx$ at onset.
 $R_f = Rx$ change from pre-onset to final myopia.
 $R_f =$ Final Rx.
 $R_m =$ Mean R.
 $c =$ rate of change constant.
 $T_o =$ age of onset.
 $a, b, d =$ arbitrary constants

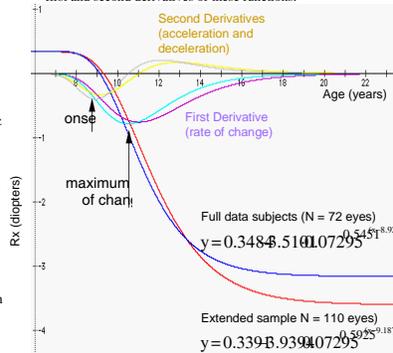
Curve Fit Examples



Mean Gompertz Models

The mean Gompertz function for 36 subjects with full data and an extended sample of 55 subjects in which some did not have complete data. When we include subjects with less complete data, the final Rx asymptote shows greater myopia. This difference is significant and is believed to be due to the inability of a limited data set to induce a strong deceleration.

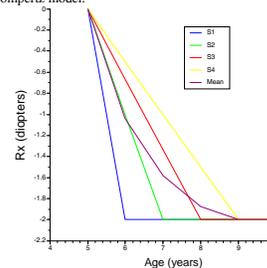
The smaller functions, shown in pastels, represent the first and second derivatives of these functions.



Group vs Individual

4. Models fit to group data cannot be used to model myopia progression in individuals. Group data, even longitudinal data normalized for time of onset, contain so much scatter that the least sum of squares is much greater. Thus, precision of the fit is much worse.

More importantly, since the myopia progression of individuals have different temporal characteristics, a model of their mean data is unlike the models of the individuals included in the analysis. This is seen in the example below. The mean of the data for the linear functions is almost exponential. This also happens if each child's data fits a Gompertz model.



Onset & Offset

2. The most dramatic feature of an individual child's full set of longitudinal data is the rapid onset of myopia progression. This suggests that myopia progression represents a triggered break from the ongoing emmetropia phase that preceded it. The other notable feature is the more leisurely pace of the slowdown in myopia progression when it stabilizes, usually by 16 years of age.

Nonsense models tell us nothing about these important features. The cosine function has equal onset and offset features. The parabolic function has no onset, starting at ultrahigh levels of hyperopia. Its offset may briefly fit the offset time characteristics of myopia progression before returning to ultrahigh hyperopia. Higher order polynomial functions can fit any data over a limited range but includes wiggles that make no biological sense.

The unrealistic model, the exponential function, has no onset, starting with ultrahigh hyperopia. We can create an onset by splining the exponential function with a horizontal line at a subjects premyopia emmetropia level. This provides an onset time but the spline function implies that the highest rate of refractive change is at the exact onset of myopia progression, which is biologically unlikely. In addition, the offset is too leisurely and stability is usually not reached until well into adulthood.

The Gompertz function and a variety of flexible asymmetric growth functions provide onsets and offsets that fit the data well and are biologically sound.

Conclusion

To create a meaningful mathematical model of the myopia progression process in individual children we must combine an understanding of the myopia progression process with statistical curve fitting techniques.

Acknowledgements

Thanks to Jane Gwiazda, Richard Held, Li Ming Dong, Tom Norton, Leslie Hyman, and Jim Comerford for discussions that led to many of these ideas. This work was supported by NIH EY01191.

References

1. Thorn F, Gwiazda J, Held R (2005) Myopia progression is specified by a double exponential growth function. Opt Vis Sci. 82, 286-297.
2. Gompertz, B. (1825) On the nature of the function expressive of the law of human mortality and on a new mode of determining the value of life contingencies. Phil. Trans. Royal Soc. London, pt.1, 513-583.
3. Yin X, Goudriaan J, Lantinga EA, Vos J, Spietz H (2003) A flexible sigmoid function of determinate growth. An Botany. 91, 361-371.

The development of myopia in adolescent after discontinuation of overnight orthokeratology.

Xiao Yang, Dongmei Cui, Huarong Wang, Binglan Fang, Junwen Zeng

State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, China.

Corresponding author: Junwen Zeng, e-mail: optzoc@gmail.com

INTRODUCTION

Orthokeratology (Ortho-K) treatment effects a rapid reduction in myopia. It is logical that questions have arisen regarding the effect this process might have on myopic progression. However, it is difficult to determine the myopic progression after wearing lens, because the corneal shape and refractive error have been changed. It has been reported that after two weeks discontinuing lens wear, the effects would recover completely. If Ortho-K lens wear is discontinued enough time and the change of refractive errors is compared between recovery and baseline, thus the myopic progression can be evaluated.

PURPOSE

This study is to determine the refractive and corneal topographic change after discontinuation of orthokeratology lenses for one month. Thus to evaluate the degree of development of myopia in adolescent after wearing Ortho-K lens overnight for 42 months.

METHODS

After forty two months of treatment by Ortho-K lens overnight wear, 38 eyes of 20 subjects (average age is 13.5 ± 3.82 yrs) were required to discontinuation for one month. Refractive error, corneal curvature in the central topography and unaided visual acuity were measured at baseline, 42 months of treatment and 1 month after discontinuing lens wear.

RESULTS

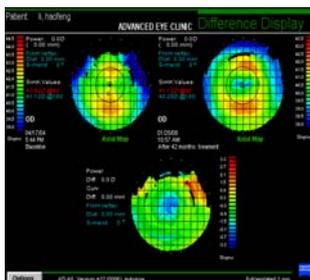


Figure 1. The difference of corneal topography between the baseline and 42 months treatment of orthokeratology.

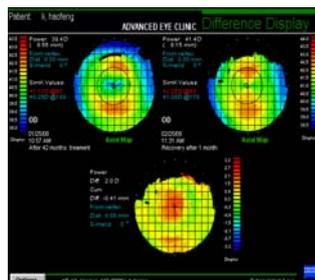


Figure 2. The difference of corneal topography between the treatment and the recovery after one month of no lens wear.

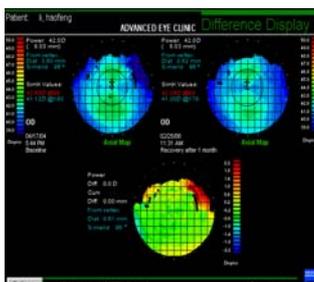


Figure 3. The difference of corneal topography between the baseline and the recovery after one month of no lens wear. The corneal topography recovered fully after discontinuing lens wear for one month.

Figure 4

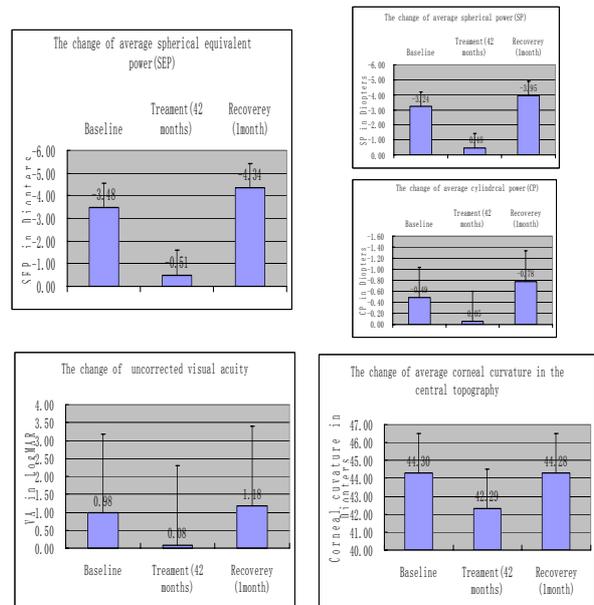


Figure 4 show the average spherical equivalent power (SEP), spherical power (SP), cylindrical power (CP), average corneal curvature in the central topography and uncorrected visual acuity at baseline, 42 months of orthokeratology treatment and 1 month after discontinuing lens wear.

The baseline of SEP is -3.48 ± 1.08 D. After discontinuing lens wear for one month, SEP increase to -4.34 ± 1.17 D ($p=0.02$). Compared with the baseline of corneal curvature in the central topography (44.30 ± 2.21 D), there is no significant change after discontinuing lens wear for one month (44.28 ± 2.16 D, $p=0.79$). The corneal topography recovered fully after one month of no lens wear.

CONCLUSIONS

As the corneal topography recovered fully after discontinuing lens wear for one month, it is supposed that the increase of refractive error is because of the progression of myopia after 42 months wear. But the progression is so slight. From this point, it seems orthokeratology can control the progression of myopia in adolescent to some extent.

REFERENCES

1. Cho P, Cheung SW, Edwards M. The longitudinal orthokeratology research in children (LORIC) in Hong Kong: a pilot study on refractive changes and myopia control. *Curr Eye Res* 2005; 30: 71–80.
2. Soni PS, Nguyen TT, Bonanno JA. Overnight orthokeratology: refractive and corneal recovery after discontinuation of reverse-geometry lenses. *Eye Contact Lens* 2004; 30: 254–262.
3. Barr JT, Rah MJ, Meyers W, Legerton J. Recovery of refractive error after corneal refractive therapy. *Eye Contact Lens* 2004; 30: 247–251.
4. Swarbrick HA. Orthokeratology review and update *Clin Exp Optom* 2006; 89: 3: 124–143

This study was supported by national natural science grant (30572005), China, and Guangdong province natural science grant (7301441), China. There is none Commercial Relationships with this study.

Corresponding address: 54 Xianlie Road, Zhongshan Ophthalmic Center, Guangzhou, China 510060
 Corresponding email address: optzoc@gmail.com, yangxiaoc3366@gmail.com
 Corresponding author: Junwen Zeng