Can current models of accommodation and vergence predict accommodative behavior in myopic children?

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Abstract

Investigations into the progression of myopia in children have long considered the role of accommodation as a cause and solution. Myopic children show high levels of accommodative adaptation, coupled with accommodative lag and high response AC/A (Accommodative convergence per diopter of accommodation). This pattern differs from that predicted by current models of interaction between accommodation and vergence, where weakened reflex responses and a high AC/A would be associated with a low not high levels of accommodative adaptation. However, studies of young myopes were limited to only part of the accommodative vergence synkinesis and the reciprocal components of vergence adaptation and convergence accommodation were not studied in tandem. Accordingly, we test the hypothesis that the accommodative behavior of myopic children is not predicted by current models and whether that departure is explained by differences in the accommodative plant of the myopic child. Responses to incongruent stimuli (-2D, +2D adds, 10 prism diopter base-out prism) were investigated in 28 myopic and 25 non myopic children aged 7 to 15 years. Subjects were divided into phoria groups- exo, ortho and eso based upon their near phoria. The school aged myopes showed high levels of accommodative adaptation but with reduced accommodation and high AC/A. This pattern is not explained by current adult models and could reflect a sluggish gain of the accommodative plant (ciliary muscle & lens), changes in near triad innervation or both. Further, vergence adaptation showed a predictable reciprocal relationship with the high accommodative adaptation, suggesting that departures from adult models were limited to accommodation not vergence behavior.

Keywords: Accommodative adaptation, Vergence adaptation, Myopia, AC/A

1.0 Introduction

1.1 Myopia and Accommodation

Myopia has reached epidemic levels in certain groups in a number of Asian countries. Morgan, Ohno-Matsui, & Saw (2012) points out that 80 to 90% of school completers in the urban areas of many Asian countries such as Hong Kong, China and Japan are myopic. Myopia is often defined by its time of onset; congenital accounting for about 5% (Banks, 1979); early onset myopia appearing in the school aged years and late onset found typically in older teenagers often in university or college (Baldwin, 1990). Human investigations show that myopia also results from excessive axial length of the eye with the vitreal chamber accounting for most of the growth (Larsen, 1971). Accommodation has been viewed as a possible source of progressing myopia for well over a century (see review - Sivak, 2012). Early thinking was based upon the idea that the prolonged accommodation resulting from near work acted to increase the axial length of the eye. This led to preventive strategies such as bifocals, eye exercises, and pharmacological investigations, as an attempt to alleviate myopic progression by reducing accommodative activity. Research investigations failed to find a clinically significant effect of bifocals on myopia progression (reviewed in Walline et al, 2011, Sivak, 2012). Controlling accommodation with bifocals re-appeared following extensive study of the role of hyperopic defocus as a key factor in myopia development. A multitude of animal species have shown that hyperopic retinal defocus may trigger axial elongation resulting in myopia, provided they were studied in their early days or weeks of life, or the eye defocused in a direction which required increased axial growth in order that the retina was conjugate with the point of regard (Schaeffel, Glasser, & Howland, 1988;Troilo & Wallman, 1991; Irving, Callender, & Sivak, 1991; Smith & Hung, 1999; Wallman & Winawer, 2004). Accommodative lag has been considered a possible source of hyperopic defocus. Myopic children show reduced steady state accommodative response under monocular viewing conditions (Berntsen et al., 2011;Mutti et al., 2006) or when viewing thorough full correction (Berntsen et al., 2011, Nakatsuka., et al., 2005) or when accommodation was stimulated using minus lenses (Gwiazda et al., 1993;Gwiazda et al., 1995a). Further, myopic children also show an increased variability of accommodation compared to

emmetropes (Langaas et al., 2008; Sreenivasan, Irving, & Bobier, 2011). A few studies have suggested sensory differences such as higher blur detection thresholds and higher depth of focus (Jiang & Morse, 1999; Rosenfield & Abraham-Cohen, 1999; Vasudevan, Ciuffreda, & Wang, 2006) to explain the larger accommodative error observed in myopes. This then pointed to the application of bifocal or progressive lenses - now as a means to reduce hyperopic defocus rather than prolonged accommodation. Results from carefully controlled trials find only very small albeit significant changes in myopia progression (reviewed in Walline et al, 2011, Sivak, 2012). However, several studies point to greater success when the bifocal was worn by a child having reduced accommodation and/or high esophoria (Goss & Grosvenor., 1990; Fulk, Cyert, & Parker, 2002;Gwiazda, 2011).

The accommodation and vergence ocular motor systems provide focused and aligned retinal images that facilitate normal functioning of the visual system. In children, as in primates in general, accommodation and vergence are tightly linked through the neural cross-links accommodative vergence (AC/A i.e. accommodative convergence per diopter of accommodation)(Alpern & Ellen, 1956a;Alpern & Ellen, 1956b) and vergence accommodation (CA/C i.e. convergence accommodation per diopter of convergence) (Fincham & Walton, 1957). Further, both accommodation and vergence undergo adaptation when viewing is prolonged (Schor, Kotulak, & Tsuetaki, 1986; Schor, 1986;Hung & Ciuffreda, 1999;Semmlow & Yuan, 2002;Hung & Ciuffreda, 1991;Maxwell, Tong, & Schor, 2012). This behavior is summarized in Figure 1.

< INSERT FIGURE 1 HERE>

If the accommodative behavior of myopic children is to be fully understood, then the interaction of accommodation with other parameters within the accommodative vergence synkinesis needs to be examined. A number of associated parameters such as accommodative adaptation and AC/A have been examined in addition to accommodative lag. Studies that looked at accommodative adaptation or its manifestation as near induced transient myopia (Ciuffreda & Wallis, 1997) have consistently reported that myopic children have high levels of accommodative adaptation (Ciuffreda & Wallis, 1997; Gwiazda et al., 1995b;Woung et al., 1993;Strang, Winn, & Gilmartin, 1994) . Clinical investigations which looked at phorias, among other standard optometric tests found a strong relationship between high esophoria at near testing distances and the development

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and progression of myopia (Goss, 1990;Goss & Zhai, 1994;Goss & Jackson, 1996). This then strongly suggests that the AC/A would be high as well (Scheiman & Wick, 2002). Direct measures of the AC/A, measured using the gradient or calculated method (Gwiazda, Grice, & Thorn, 1999; Gwiazda, Thorn, & Held, 2005) or by changing accommodation in a Badal set up (Mutti et al., 2000a) show elevated ratios in young myopes. There is disagreement whether the ratio is high prior to myopia onset (Gwiazda, Thorn, & Held, 2005) or whether it occurs only after myopia onset (Mutti et al., 2000a). Also the origin of the high AC/A has been debated. Mutti and associates (Mutti et al., 2000a) hypothesized that the most likely explanation would be a difference in the accommodative plant (i.e. ciliary muscle & crystalline lens) between myopes and non myopes. They postulated that accommodation could become attenuated if the crystalline lens in myopes where to exert greater force on the choroid, thereby attenuating its transduction effect in accommodation. The evidence is not direct but comes from inferences taken from their data that shows different patterns of changes in crystalline lens development in myopes and non myopes (Zadnik et al., 1995). Recently, myopes have been found to show a thickened ciliary muscle (Buckhurst et al., 2013;Lewis et al., 2012;Lossing et al., 2012). Specifically, the posterior fibres are thickened in myopia while apical fibres are thicker in hyperopia (Pucker et al., 2013). However evidence indicating whether accommodation is attenuated proportionally due to plant differences has not been found (Schultz et al., 2009).

In summary, the accommodative behavior of young myopes shows high accommodative adaptation coupled with reduced reflexive properties and a high AC/A. Examination of Figure 1 shows some inconsistencies. The findings of a high AC/A, reduced accommodative responses coupled with a high degree of accommodative adaptation does not fit the expected innervational patterns predicted by these models where high accommodative adaptation would result in reduced AC/A. Also it is unclear how a high level of accommodative adaptation could result from reduced reflexive accommodation. However, the findings have been taken from studies where often only one parameter was examined (e.g.) reflex accommodation. Furthermore, there was no data on vergence adaptation and CA/C measures to put the accommodative measures in context.

1.2 Our previous investigations using near adds in myopic children

Our lab developed a research design where we began a detailed investigation of the accommodative vergence synkinesis in adults (Sreenivasan, Irving, & Bobier, 2008) and myopic children with normal near phorias (Sreenivasan, Irving, & Bobier, 2009) to +2.00D near adds, which have been prescribed in clinical trials of myopia prevention (e.g. Gwiazda et al., 2003) We recognized that this served as a non-congruent stimulus (change in binocular accommodation with no direct change to vergence) that would challenge the adaptive components of convergence and accommodation and also provide information regarding how school aged myopes adjusted to these near adds. The basic experimental design consisted of prolonged viewing at 33cm with and without +2D near addition lenses for 20 minutes. Accommodation was measured using a photorefractor (Power Refractor, Multichannel systems, Germany). Vergence adaptation in response to the near adds was measured by intermittent phoria measures (Modified Thorington technique) (Sreenivasan, Irving, & Bobier, 2009).

Under natural viewing conditions (i.e. with distance correction only), we found that myopic children exhibited higher accommodative lags (Sreenivasan, Irving, & Bobier, 2009); which were sustained over the 20 minutes. The application of a +2D near addition lens clamps vergence as it were, and reduces the stimulus to accommodation in each eye. The model (Fig.1) predicts that reduced reflex accommodation leads to a lower tonic level (as tonic or adaptive component receives input from the reflex system). Viewing through +2D near adds reduced the lag similar to other reports (Shapiro, Kelly, & Howland, 2005;Seidemann & Schaeffel, 2003;Rosenfield & Carrel, 2001) and reduced the degree of accommodative adaptation in both groups (Sreenivasan, Irving, & Bobier, 2009). Further, the relaxation of accommodation and accommodative convergence through the near +2D add showed elevated AC/A ratios in myopes confirming previous investigations (Mutti et al., 2000a; Gwiazda, Thorn, & Held, 2005). The relaxation of accommodation and resulting accommodative divergence seen at the summing junction (indicated by A in Fig.1) adds to reflex disparity convergence, the sum of which is then available to be replaced by tonic vergence. A phoria measure, which opens the loop of disparity vergence, would initially indicate an increased exophoria (or reduced esophoria) with a need for increased accommodative convergence. The decay of this lens-induced phoria over time

would identify the tonic vergence adaptation. Tonic vergence adaptation was enhanced by a resumption of binocular vision following phoria measures so that both disparity vergence and accommodative vergence summed at A to drive the adaptation. The increased exophoria induced by the +2D was adapted by each group, but myopes showed a significantly lower magnitude of vergence adaptation than the controls.

Contrary to plus adds, -2D adds will increase the accommodative demand and accommodative convergence, we thereby pursued to further examine vergence and accommodative adaptation between myopes and emmetropes. Further, we aimed to look at possible gradations in the effect by investigating both accommodative and vergence adaptation in myopes and controls with varying degrees of AC/A. Given that individual AC/A ratios could be identified from near phoria measures we recruited a large sample of subjects where AC/A ratios were distributed between near phoria measures: *"normophores"*- 0 to 4Δ exo; significantly exophoric > 6Δexo and significantly esophoric >2Δeso. We repeated our previous testing designs (Sreenivasan, Irving, & Bobier, 2009) where subjects sustained fixation for 20 minutes under conditions of natural viewing (i.e. through best corrective lenses only) where accommodation and vergence experienced congruent demands and using a set of incongruent target demands, using near adds and prism. We have already reported on the results from the natural viewing without the adds (Sreenivasan, Irving, & Bobier, 2012). We found that AC/A ratios and accommodative adaptation were significantly higher in the myopic children during natural viewing through corrective lenses.

1.3 Current Investigation

The following investigation provides the final phase of the study where we look further into the question of whether elements in the myopic child's accommodation and vergence profile differ significantly from those modeled based upon adults. First, we chose to clamp vergence and vary accommodation using both +2D lenses and -2D lenses where the latter would provide increased accommodation and thereby, adaptation and, be driven over a more linear range (Morgan, 1946). Secondly, we wanted to clamp accommodation (open-loop) and measure vergence changes in response to viewing through a 10Δ (prism-diopter) base-out (BO) prism at 4M. Thus tonic vergence would be measured directly and the stimulus would now be retinal disparity. Finally, by measuring properties of

accommodative and vergence adaptation as well as the gain of the cross links (AC/A and CA/C ratios), we would test the hypotheses that the unique pattern of accommodative behavior of myopes, may be explained by reduced gain of the accommodative plant (Mutti et al., 2000b;Berntsen et al., 2011).

2.0 Methods

As discussed above, the first phase of this investigation involving viewing through best corrective lenses alone (i.e. without either near adds or prism). The results for this condition have been described elsewhere (Sreenivasan, Irving, & Bobier, 2012). However, we will describe that component as well for context. The study protocol was approved by the University of Waterloo ethics review board and adhered to the tenets of the Declaration of Helsinki. Participants were recruited from the clinic database at the School of Optometry and Vision Science, University of Waterloo. Informed consent (parents) and assent (children) were obtained after verbal and written explanations of the procedures involved in the study.

A total of 53 children (28 myopic and 25 emmetropic; 57.5% female) between the ages of 7 and 15 years were examined. All children had either myopic refractive error between -0.75 and -6 D or emmetropia defined as refractive error between +0.5 and +1.5 D determined using cycloplegic refraction (performed using 1% Tropicamide) astigmatism < 1D; anisometropia < 1D; best corrected visual acuity of at least 6/6 in each eye; were non-strabismic, had normal accommodative and fusional amplitudes through best corrective lenses; and had no history of bifocal/PAL use in the past. The range of refractive error in the "emmetropic group" was set to ensure that participants were clearly not myopic and therefore confirm distinct refractive differences between the study groups.

For the near add protocol, children were divided into three phoria groups based on their phoria through distance-corrective lenses at 33cm (Table 1). Children were classified as *"normo-phores"* (mean near phoria between 0-4 exo), exophores (>6 exo) or esophores (>2 eso; Table 1). Throughout the paper, the different phoria and refractive groups have been abbreviated as follows: The first letter corresponds to the refractive error (M for Myopes and E for emmetropes) while the second letter represents the phoria group (X for exophores, E for esophores and N for normophores).

2.1 Instrumentation and procedure

The overall study design involved 3 separate visits where measures were taken over 20 minutes while subjects viewed through a combination of their distance correction and either +2D near addition lenses or -2D addition lenses as part of the lens adaptation study and a third visit for the tonic vergence and its adaptation with 10Δ base-out prism. The instrumentation and procedure used for quantifying adaptation were similar to previous studies (Sreenivasan, Irving, & Bobier, 2009;Sreenivasan, Irving, & Bobier, 2008;Sreenivasan, Irving, & Bobier, 2012). For all conditions, participants sat in total darkness for 3 minutes prior to collecting data to dissipate any effects of previous near work and allow the accommodation and vergence system to return to their resting states (Wolf, Ciuffreda, & Jacobs, 1987).

2.2 Measurement of Vergence Adaptation through +/- 2D near adds

Trial lenses were inserted at a distance of 12 mm from the participants' eyes and the trial frame was adjusted for near inter-pupillary distance to reduce any prismatic effect. Following this, measurements of near phoria were obtained at 33 cm through distance corrective lenses to establish the "baseline". Phoria measures were taken using the modified Thorington technique. The technique has been shown to be valid, and repeatable (to within 1.5PD) for measurements of phoria in children (Sreenivasan, Irving, & Bobier, 2009;Sreenivasan, Irving, & Bobier, 2008;Sreenivasan, Irving, & Bobier, 2012). Each recorded phoria was an average of 3 measures. Subsequent to the baseline measurement, participants were instructed to close their eyes and +2D or -2D lenses were binocularly added over their correction. The examiner confirmed clear vision through the adds when fixation was monocular and performed a measure of phoria (after occlusion for approximately 10 seconds) before permitting any binocular viewing through the addition lenses. This response was defined as the lens-induced phoria for which adaptation was to be quantified.

Children were then instructed to watch a cartoon movie that was played at a distance of 33 cm and phoria measures were repeated after 2, 4, 6, 8, 10, 15 and 20 minutes of near fixation. Participants were instructed to report any blurriness of vision anytime

during the session. Phoria (vergence) adaptation curves defined the vergence adaptation to either the + or – 2D add.

2.3. Measurement of accommodation and accommodative adaptation

All accommodative responses were obtained using the *monocular mode* of an eccentric infra-red (IR) photorefractor (PowerRefractor, Multichannel Co, Reutlingen, Germany; see Choi et al., 2000;Gekeler et al., 1997;Schaeffel, 2002) by averaging the data over a duration of 5 sec at a sampling frequency of 25 Hz. These were taken coincident with the phoria measures. The high contrast (85%) targets used for near (+/- 2D near adds) adaptation conditions were similar to previous studies (Sreenivasan, Irving, & Bobier, 2009;Sreenivasan, Irving, & Bobier, 2008;Sreenivasan, Irving, & Bobier, 2012). The measures obtained from the PowerRefractor were calibrated based on individual calibration equations using a two-step protocol similar to previous studies (Sreenivasan, Irving, & Bobier, 2008;Sreenivasan, Irving, & Bobier, 2012).

Accommodative adaptation was calculated by measuring tonic accommodation (open-loop accommodation) before and after the sustained task (cartoon). The accommodative system was rendered open-loop by instructing participants to fixate a low spatial frequency (0.2 cpd) difference of Gaussian target' monocularly at 4M (left eye occluded). Such targets block medium and high spatial frequency information required for accommodation and has been considered to be an effective stimulus to open the accommodative feedback loop (Kotulak & Schor, 1987).

2.4. Adaptation of Tonic Vergence with 10Δ Base-Out

Subjects were recruited from the Near Add study. They were categorized in the same manner as the near lens study (Figure 2). However, as described below, a number of children were unable to do this testing (see data analysis section).

< Figure 2 here>

Measurement of tonic vergence (TV) position requires both accommodation and vergence to be open-loop. To facilitate this, TV was determined by measuring horizontal heterophoria (modified Thorington technique) at 4M through 0.5 mm pinhole pupils placed in a trial frame and centered before the pupils. TV measures were performed using a

flashing technique similar to that previously conducted through the near addition lenses (Sreenivasan, Irving, & Bobier, 2008). TV was defined as the average of the three responses and tonic vergence adaptation was quantified by measuring changes in tonic vergence. After a baseline measure of TV through distance correction, the 10Δ BO prism was added in front of the occluded left eye. Tonic vergence was measured prior to any binocular viewing through the prism and this represented the induced TV for which adaptation was to be quantified. Binocular fusion/suppression through the prism was then evaluated by presenting monocular Nonius lines using polarizing glasses. Participants with suppression/diplopia through the prisms were excluded from the study.

Measures of binocular open-loop accommodation were taken before and after the insertion of the prism and the induced change was considered as convergence-accommodation (because other components of accommodation were either eliminated (blur) or kept constant (proximity). Further, since tonic changes in accommodation (accommodative adaptation) could influence open loop accommodative measures and therefore confound the CA measures, we also measured tonic accommodation before and after sustained fixation, similar to the procedure described in the "near add" section.

2.5 Measurement of cross-link (AC/A & CA/C) ratios:

Cross-link ratios were measured on a separate day in all participants. AC/A ratios were measured by altering accommodative demand using ophthalmic lenses (Gradient AC/A) and measuring the changes to phoria and accommodation under monocular viewing conditions. Spherical lenses ranging from +2 to -2D (in 1D steps) were binocularly introduced over corrective lenses and the corresponding changes to phoria and monocular accommodation were measured through each lens addition. The slope of the linear fit with induced lenses and resultant change in phoria defined the stimulus AC/A ratio. Response AC/A ratios were calculated by using both the slope of change in accommodative vergence and the slope of change in monocular accommodation.

The stimulus CA/C ratio was measured by changing disparity using base-out prisms, when the accommodative feedback loop was opened using a 0.2 cpd difference of Gaussian target. This target renders accommodation open loop; yet, contains sufficient disparity cues to stimulate motor fusion (Kotulak & Schor, 1987). Disparity was increased in 4 prism diopter steps (0, 4, 8, 12) and the concomitant change in accommodation was

measured once the subject reported fusion through the prism. The stimulus CA/C ratio was calculated from the slope of the linear fit plotting induced convergence and the resultant change in accommodation. Response CA/C was not measured because vergence errors are usually less than 1PD, (Ogle, 1950) hence stimulus and response CA/C ratios are typically similar.

2.6 Data Analysis

Repeated measures analyses of variance (RM-ANOVA) was used to determine the effect of add/prism condition and time on phoria (& TV) response. Statistically significant main effects were further examined using post-hoc tests. Data analysis was performed using STATISTICA 6.0 (StatSoft, Inc, USA). Changes in phoria induced by the near adds and those of tonic vergence induced by the base-out prism were fit with exponentials. The resulting parameters (magnitude and completeness of adaptation) from those fits were used to quantify adaptation similar to past studies (Sreenivasan, Irving, & Bobier, 2009;Sreenivasan, Irving, & Bobier, 2008;Sreenivasan, Irving, & Bobier, 2012). The "magnitude" of adaptation was defined as the overall change in phoria or tonic vergence after 20 min fixation through the adapting stimulus (adds or prism) while the "completeness" of adaptation, was defined as the degree to which the adapted phoria or vergence measure had returned to the habitual level through best corrective lenses. Curve fitting and analysis were performed using Graphpad software (Graphpad Inc, USA).

2.6.1 Subject attrition and resulting data analysis

Near add study

Of the 53 recruited subjects, three myopes were excluded from the overall data analysis due to complaints of blurred vision through the near adds (n=2) and pupil size that was too small for photorefractive measurement (n=1).

Prism study

Of the 50 remaining subjects, 11 subjects (eight emmetropes and 3 myopes) were unable to overcome the 10Δ base-out prism and complete the tonic vergence measure and generate convergence accommodation. These subjects were found to experience prolonged diplopia or suppression during prism viewing or experienced difficulty viewing through the pinholes. The details of the numbers within each phoria group are shown in figure 2.

The greatest attrition comes from emmetropes who could not fuse viewing through the 10 base-out prism. While the reason for this preponderance in emmetropes is unclear, refractive error does not seem to be a factor since the mean refractive error in the non-fusing emmetropes (0.50±0.13D) was similar to those that were able to fuse the prism (0.43±0.06D). Examination of the baseline tonic vergence (prior to prism exposure) in non-fusers shows an average of 0.2eso (SD= 2.1) compared to the overall mean of 2.7Δeso (SD=2.1) Thus the attrition was not directly related to the magnitude of their tonic vergence. On the other hand, those myopes unable to perform the PRISM condition showed a mean tonic vergence (2.6 exo ±2.0) compared to a mean of 1.58 eso (±2.8△) for those included in the analysis. Given this result (differences in TV) we studied a sub group that had similar and normal tonic vergence characteristics (see section 3.4).

In this paper, we report data analysis conducted on the subjects who completed all conditions (17 controls and 22 myopes). However the adaptation results (or the conclusion) in the add condition is similar when analyze 25 myopes and 25 controls or whether we only chose those that completed all conditions. The mean spherical equivalent (SE) refractions for the group of children with complete data sets were +0.43D±0.06D (min SE=0 and max SE=1D) in emmetropes and -2.03±0.4D (min SE=-3.5D and max SE=-0.5D) in myopes.

3.0 Results

3.1. Cross-link ratios

The response AC/A ratios differed between the near phoria categories (one-way ANOVA - AC/A: P=0.02) in each group, as would be expected, where esophores showed the highest AC/A and exophores the lowest (ME vs. MX: P=0.04; EX vs. EE: P=0.10). Further, consistent with the past literature and our past studies, myopes as a group showed significantly larger AC/A than emmetropes (two-way ANOVA; effect of refractive group P=0.005; Fig 3). However, the slopes of CA/C (D/Δ) ratios were found to be similar between the refractive groups and near phoria categories category (MX=0.06±0.01; MN=0.04±0.02; ME=0.04±0.03; EX=0.04±0.01; EN=0.08±0.05; EE=0.05±0.04: two-way ANOVA main effect of refractive group-P=0.34).

<FIGURE 3 HERE>

3.2 Accommodative adaptation to closed-loop accommodation (near adds at 33 cm) and open-loop accommodation (10BO prism at 4M)

For all conditions, accommodative adaptation was defined as the difference between pre and post-task tonic accommodation (Fig 4). The type of add condition significantly influenced the amount of accommodative adaptation (P<0.0001) such that greater adaptation was seen through minus adds compared to plus adds. Myopic children showed significantly greater accommodative adaptation compared to emmetropic children after fixation through minus adds (P=0.01) but similar amount of adaptation after sustained viewing through plus add lenses (P=0.60)

In the +2D condition, myopic esophores showed significantly higher (more myopic) accommodative adaptation compared to other groups (P<0.01; Fig 4a). In the minus add condition, exophores showed significantly lower accommodative adaptation compared to esophores in both refractive groups (EX vs. EE: P=0.01;MX vs.ME: P=0.002; Fig 4b) but only compared to normophores in the myopic category (MX vs.MN: P=0.01;EXvs. EN=0.09).

When fixation was sustained by watching a cartoon movie at 4M through 0.5mm pinholes that opened accommodative loop, accommodative adaptation was still significantly greater in myopic children compared to emmetropes (Emm=0.04±0.10; Myo= -0.28±0.08; Fig 4c; P=0.04).

< INSERT FIGURE 4 AROUND HERE>

3.3 Phoria adaptation to plus and minus addition lenses

The mean habitual near phorias (Table 1) in each phoria category and refractive category were similar (P=0.90) between the plus add and the minus add sessions performed on different days, suggesting good repeatability of near phoria. For any given phoria category, the habitual near phoria was statistically similar between the two refractive groups (P value at least >0.1 between groups).

3.3.4 Plus addition lenses

Plus addition lenses relaxed accommodation and accommodative convergence resulting in lens-induced relative exophoria which reduced with sustained fixation in all

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children, similar to previous studies (North & Henson 1985; Sreenivasan, Irving, & Bobier, 2009). Exponential vergence adaptation curves showed that completeness of adaptation significantly differed as a function of refractive group (Fig5, $P<0.0001$). For each phoria category, myopic children showed significantly less adaptation compared to emmetropic children (Post-hoc analysis: EX vs.MX: $P<0.0001$; EN vs.MN: $P=0.001$; EE vs.ME: $P=0.006$).

The main effect of phoria category was significant (Main effect $P<0.0001$), where exophores displayed significantly higher completeness compared to normophores ($P=0.01$) and esophores ($P<0.001$). The interaction between phoria category and refractive type was also significant (Fig 6, $P=0.006$), demonstrating that the phoria type had a greater effect on emmetropes compared to myopes.

< INSERT FIGURE 5 AROUND HERE>

3.3.5 Minus adds

Minus adds induced accommodation and accommodative convergence. As a result, a relative esophoria initially resulted, which adapted (decreased) significantly over time in all groups (Main effect of time in each group: $P<0.05$) except emmetropic exophores (Fig 5; $P=0.33$). We found a significant main effect of phoria category on phoria adaptation to minus adds as a function of magnitude ($P<0.0001$) and completeness ($P<0.001$; Fig 6). Esophores showed significantly higher magnitudes and completeness of adaptation compared to normophores ($P<0.001$) and exophores ($P<0.0001$) in both refractive groups. The main effect of refractive type was non-significant for either parameter of adaptation ($P=0.08$ for magnitude and $P=0.14$ for completeness- Fig 6). Additionally, the interaction between phoria category and refractive error was also non-significant (Fig 6, $P=0.70$).

3.3.6 Comparison between plus and minus add conditions

Repeated measures ANOVA was performed to compare the completeness of phoria adaptation between the plus and minus add conditions in all groups. A highly significant main effect of add condition ($P<0.0001$), interaction between add condition and type of phoria category ($P<0.0001$), and a significant interaction between add condition and refractive type ($P<0.0001$) were observed. These results indicate that there is an asymmetry in phoria adaptation between the plus and the minus add conditions which is dependent

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upon both the category of near phoria and the refractive group (Fig 6). Emmetropic exophores ($P<0.0001$; difference in completeness between add conditions=108%; Fig 6) and myopic esophores ($P<0.0001$; difference in completeness=42%; Fig 6) showed the greatest asymmetry in adaptation between the +2D/-2D add conditions. However, the other groups MX ($P=0.06$) and EE ($P=0.40$) did not show statistically significant differences in the completeness of adaptation between the add conditions (Fig 6).

< INSERT FIGURE 6 AROUND HERE>

In an effort to understand the asymmetric adaptation pattern to near adds, we determined the fusional vergence demand required for each subject at the onset of viewing through either the plus or negative add. This was calculated by determining the amount of fusional divergence or convergence required to overcome the resulting eso or exo phoria respectively. For both parameters of adaptation, magnitude (Fig 7) and completeness, we found a significant correlation ($P<0.05$) suggesting that the magnitude of adaptation is less when the near add decreases rather than increases the phoria (Magnitude: Emm: +2D and -2D combined: $P<0.0001$; overall $r=-0.91$; $r^2=0.83$; Myo: $P<0.0001$; $r=-0.85$; $r^2=0.72$).

< INSERT FIGURE 7 AROUND HERE>

3.4 Tonic vergence adaptation to 10 BO prism

Fig. 8 (A) shows the mean changes to tonic vergence through 10 Δ BO in the emmetropic and myopic groups. Differences in the baseline tonic vergence through corrective lenses were non-significant between the refractive groups ($P=0.15$). The addition of 10 Δ BO significantly increased exophoria ($P<0.001$) whose magnitude was also similar between the two refractive groups (E=8.92±0.20; M=8.71±0.33; $P=0.50$). Prolonged binocular fixation significantly reduced the prism-induced exophoria ($P<0.001$) in myopic and emmetropic children. This is taken to be indicative of a change in tonic vergence to a more convergent position, reflecting vergence adaptation. The exponential decay curves in the myopic children showed a significantly reduced magnitude (E=6.30±0.31; M=5.01±0.42; $P=0.03$) and completeness of vergence adaptation (E=70.71±3.20; M=58.01±4.40; $P=0.04$) compared to emmetropes. Most of the difference appears to be in the final magnitude not the early rate of change when the slope is highest.

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< INSERT FIGURE 8 AROUND HERE>

In both refractive groups, the magnitude of vergence adaptation significantly correlated with the fusional vergence demand created by the prism and their habitual tonic vergence position (Pearson r= -0.58, r^2=0.34; P=0.01; M: r=-0.43, r^2=0.19; P=0.03). This suggests that the starting position (i.e. baseline tonic vergence) influences the degree of vergence adaptation to a BO prism such that a lower demand on the fusional vergence created by a convergent (eso) vergence posture resulted in a smaller degree of adaptation. Given this relationship, the reduced magnitude and completeness of adaptation observed in the myopic group (Fig 8) could result from more children with baseline convergent vergence posture compared to emmetropes. To remove the bias of fusional vergence, we defined a normal tonic vergence category by transposing the vergence settings into distance phoria measures where norms exist (Morgan, 1944; For Children: Lyon et al., 2005). These distance phoria measures were then converted to tonic vergence (TV) using the formulae {predicted TV= distance phoria+ AC/A*(tonic accommodation–depth of focus)}, proposed by O'Shea et al (1990) and Rosenfield and Cuiffreda (1990). Children were divided into different tonic vergence categories: eso (TV=>4Δ eso), exo (TV=<1Δ Exo) or normal (TV=1Δ eso to 3Δ exo). Based on this grouping schema, we had 27 children with normal tonic vergence (E=13; M=14), 11 children with convergent TV (Emm=5; Myo=6) and 5 with divergent TV (E=1; M=4). Fig 9 shows responses from children with normal tonic vergence alone. It was confirmed that myopic children show significantly reduced amount (EN=6.82±0.40; MN=5.20±0.41; P=0.01) and completeness of vergence adaptation (EN=74.31±2.60; MN=58.91±4.80; P=0.01) even with normal baseline TV position. This pattern was seen despite showing the same levels of induced tonic vergence through the prism compared to emmetropes (EN=8.9±0.40; MN=8.98±0.31; P=0.92). In both cases of tonic vergence adaptation (Figs. 8 &9) convergence accommodation (open loop accommodation) varied significantly over time (P=0.004) and reduced as would be expected.

< INSERT FIGURE 9 AROUND HERE>

4. Discussion

The main findings were that myopic children showed high accommodation adaptation, high AC/A, and reduced vergence adaptation but similar CA/C ratios when compared to non-myopic children. The results are discussed below in the context of current adult models of accommodation and vergence.

AC/A measures were highest in esophores and least in exophores independent of refractive category. The presence of myopia heightened the AC/A values in all groups (Figure 3) compared with the non myopes similar to previous studies (Mutti et al., 2000a;Gwiazda, Grice, & Thorn, 1999;Gwiazda, Thorn, & Held, 2005). However, this increased AC/A in myopes was dependent upon near phoria type. Therefore, for example, the exophoric myopes did not have higher AC/A ratios compared to esophoric non myopes (Figure 3). Using a related design and same group of children, but without the addition of lenses or prisms (i.e. best corrective lenses), we have previously shown a similar relationship with accommodative lag to that of the AC/A and near phoria (Sreenivasan, Irving, & Bobier, 2012). Accommodative lags under binocular viewing conditions were greater in esophores compared with exophores and the presence of myopia was associated with an increased lag in both phoria groups. In the present study, we found that patterns of accommodative adaptation are influenced more by the profile of the near phoria than by the presence or absence of myopia (e.g. Minus add Figure 4).

These results are surprising based on our current understanding of models of the accommodative and vergence synkinesis (Schor, 1986;Schor & Kotulak, 1986;Schor, 1988). Adults show a pattern experimentally, where high AC/A measures are associated with reduced accommodative adaptation but low CA/C gains are coupled with high vergence adaptation (Schor & Horner, 1989). These findings are predicted in long standing models of accommodation (Schor, 1988) and lead to reciprocal relationships with cross links where a high AC/A ratio is coupled with a low CA/C (Schor & Kotulak, 1986). The high AC/A in myopes cannot be explained by reciprocal pattern of low accommodative adaptation and high vergence adaptation since the opposite has been found. Our hypothesis that the accommodative vergence synkinesis of young myopic children differs from adults in these parameters is upheld and appears to be applicable to non myopic children but to a lesser degree.

How might this differing behavior be explained? Near triad neural patterns could be altered which selectively increase the gain of the AC/A cross link. Empirical evidence from adults show that increased AC/A ratios (and decreased CA/C) ratios can be achieved by optical designs which increase the apparent interpupillary distance (Judge & Miles., 1985). However these changes are difficult to effect in comparison with vergence adaptation (Judge & Miles., 1985; Fisher & Ciuffreda, 1990) and are highly variable between individuals (Bobier & McRae., 1996). Furthermore, high gains of accommodative adaptation and AC/A cross links would not explain the high lags of accommodation found in myopic children.

Could the etiology of the findings in young myopes lie with a reduced gain in the accommodative plant (Mutti et al., 2000a)? A sluggish accommodative plant would lead to an apparent increase in the AC/A since greater accommodative effort would be required to produce the necessary accommodative response. This would lead to a proportionally greater output of accommodative convergence since the vergence plant is not affected. Current models would also predict an increase in accommodative lag with decreased gain of the accommodative plant. Whether the high tonic adaptive levels result from the increased reflexive accommodative effort to overcome the plant, or results from actual changes in the gain of accommodative adaptation is not clear. However, CA/C ratios in myopes did not significantly differ between myopes and controls. A decrease in the CA/C ratio would be expected in the case of a reduced gain of the accommodative plant. However, our results showed that the higher levels of accommodative adaptation found in myopes can be driven by both reflex accommodation and convergence accommodation. Since our measure of CA was open loop responses of accommodation, it could be inflated by greater increases in the tonic accommodation of myopes created by the CA. This point could be further examined by determining the CA output of the two groups in response to pulsed and step inputs which would avoid accommodative adaptation. Our finding that at least some non myopic children (esophores) show a pattern of high accommodative adaptation and high AC/A in itself needs further examination with respect to adult behavior.

In conclusion, in addition to their high accommodative lags, myopic children show a pattern of reduced vergence adaptation coupled with high accommodative adaptation;

however, unlike adults a higher rather than lower AC/A is found. The resulting high AC/A in myopic children cannot be explained by differing degrees of adaptation between accommodation and vergence. The underlying mechanisms explaining this behavior in myopic children would appear to result from differing neural couplings within the near triad, sluggish accommodative plant gains or combinations of the two.

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