Are high lags of accommodation in myopic children due to motor deficits?

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Highlights

1. Blur accommodation but not convergence accommodation (CA/C) is reduced in myopes.
2. Myopes show a similar rate of change in the response dynamics like the emmetropes.
3. Atypical response patterns exist with blur accommodation but decrease with age.
4. Pure sensory or motor deficit doesn’t predict the abnormal behavior in myopes.
5. Model simulation with altered sensory and motor gain predicts the myopic behavior.
Children with a progressing myopia exhibit an abnormal pattern of high accommodative lags coupled with high accommodative convergence (AC/A) and high accommodative adaptation. This is not predicted by the current models of accommodation and vergence. Reduced accommodative plant gain and reduced sensitivity to blur have been suggested as potential causes for this abnormal behavior. These etiologies were tested by altering parameters (sensory, controller and plant gains) in the Simulink model of accommodation. Predictions were then compared to the static and dynamic blur accommodation (BA) measures taken using a Badal optical system on 12 children (6 emmetropes and 6 myopes, 8-13 years) and 6 adults (20-35 years). Other critical parameters such as CA/C, AC/A, and accommodative adaptation were also measured. Usable BA responses were classified as either typical or atypical. Typical accommodation data confirmed the abnormal pattern of myopia along with an unchanged CA/C. Main sequence relationship remained invariant between myopic and non-myopic children. An overall reduction was noted in the response dynamics such as peak velocity and acceleration with age. Neither a reduced plant gain nor reduced blur sensitivity could predict the abnormal accommodative behavior. A model adjustment reflecting a reduced accommodative sensory gain (ASG) coupled with an increased AC cross-link gain and reduced vergence adaptive gain does predict the empirical findings. Empirical measures also showed a greater frequency of errors in accommodative response generation (atypical responses) in both myopic and control children compared to adults.
Progressive myopes exhibit an accommodative behavior characterized by high response lags that increase with the demand (Gwiazda et al., 1995a; Gwiazda et al., 1993; Koomson et al., 2015; Mutti et al., 2006; Nakatsuka et al., 2005), elevated response AC/A (Gwiazda, Grice, & Thorn, 1999; Gwiazda, Thorn, & Held, 2005; Mutti et al., 2000), and high accommodative adaptation (Gwiazda et al., 1995b; Sreenivasan, Irving, & Bobier, 2012). These patterns are not predicted by the currently accepted models of accommodation and vergence which suggest that a high accommodative adaptation would be associated with a low AC/A and smaller response lags (Schor & Bharadwaj, 2006; Schor, 1992). Myopes also show high steady state fluctuations (Langaas et al., 2008; Sreenivasan, Irving, & Bobier, 2011), reduced vergence adaptation (Sreenivasan, Irving & Bobier, 2012) and a large depth of focus (Rosenfield & Abraham-Cohen, 1999; Vasudevan, Ciuffreda, & Wang, 2006). Furthermore, several studies showed that the onset of myopia is associated with changes in the accommodative response (Gwiazda et al., 2005; Mutti et al., 2006). Interestingly, this abnormal behavior is associated only with progressive and not stable myopia (Abott, Schmid, & Strang, 1998; Gwiazda et al., 1995a; Jiang & Morse, 1999). Nevertheless, these patterns of accommodation do not appear to be causative because correction of the lags does not reduce the myopic progression to a significant clinical level (Berntsen et al., 2012; Gwiazda et al., 2004; Shapiro, Kelly, & Howland, 2005).

Studies on children and adults have found differences in the accommodative plant of myopes, specifically, altered crystalline lens growth (Goss et al., 1997; Jones et al., 2005; Mutti et al., 2012, 2000, 1998; Philip et al., 2014; Shih, Chiang, & Lin, 2009; Zadnik et al., 1995) along with a thick and rigid ciliary muscle (Bailey, Sinnott, & Mutti, 2008; Buckhurst et al., 2013; Jeon et al., 2012; Lewis et al., 2012; Lossing et al., 2012; Oliveira et al., 2005; Pucker et al., 2013). Previous work showed that the equatorial growth of the crystalline lens ceases earlier in myopes compared to the non-myopes (Mutti et al., 1998). They predicted that the failure of the lens to compensate for the axial growth of the eye could lead to an increased tension on the choroid and hinder accommodation. However, no study to date has shown if these anatomical differences would actually lead to an abnormal accommodative behavior. A recent investigation (Gwiazda et al., 2015) found no correlation between myopia progression and changes in the lens growth pattern. They concluded that changes in the lens thickness do not accompany or cause myopia and could be merely coincidental.

Reduced blur sensitivity was found in both young and adult myopes (Gwiazda et al., 1995a, 1993; Jiang, 1997; Schmid et al., 2002). This reduction was speculated to increase the depth of focus (DOF) thereby leading to a reduced accommodative response. In agreement, studies found a large depth of focus in myopes both objectively (Vasudevan, Ciuffreda, Wang, 2006) and subjectively (Rosenfield & Abraham-Cohen, 1999). Increased higher order aberrations were suggested to increase the depth of focus in myopes by degrading the retinal image quality, ultimately leading to an inaccurate accommodation (Charman, 2005; He et al., 2005). Furthermore, studies looking at genetic mutations in myopes found an altered behavior in the retinal processing (Morgan, Rose, & Ashby, 2014). We speculate that these mutations could influence blur processing, possibly a decreased blur sensitivity which occurs at the level of retina. Previously, accommodative sensory gain (ASG) parameter was introduced into a static model of accommodation along with the dead space operator (DOF) to account for the sensory (blur) component (Jiang, 1997). Unlike DOF, the
ASG predicted increased response lags as the stimulus demand increased, similar to the empirical accommodative measures.

1.1 Model simulations

Figure 1: Model of accommodation and vergence adapted for myopes (Adapted from Schor, 1992; Jiang, 1997, Maxwell et al., 2010). The control mechanism of accommodation and vergence is characterized by a pulse step innervation. For accommodation, response to a step stimulus is initiated by an open-loop pulse followed by a closed loop step system that code for the dynamic characteristics and position respectively. The closed loop step system is predicted to be under the influence of an internal feedback to avoid errors in the response. The interactions between accommodation and vergence are characterized by pulse and step cross-link. For simplicity, we have not shown the internal feedback and the pulse cross-link mechanism. The cross-links CA and AC are approximated empirically using measures of CA/C and AC/A respectively and are represented as gains in the model. We also adapted the ASG (Jiang, 1997) into this model to address the blur detection system of accommodation. DOF: Depth of focus; PA: Panum’s area and ASG: Accommodative sensory gain.

In summary, empirical studies suggest that the abnormal pattern of accommodation could either reflect a motor deficit (e.g. a rigid lens and/or a sluggish ciliary muscle), or sensory deficit (i.e. reduced blur sensitivity) or perhaps a combination of both. A Simulink model (MATLAB) was devised, as shown in figure 1, by including the ASG component into the current model of accommodation proposed by Schor and his associates (Maxwell,Tong & Schor, 2010; Schor & Bharadwaj, 2006; Schor, 1992). Simulations were carried out to determine if these deficits would
predict the abnormal accommodative behavior. Table 1 below lists the outcomes of the model adjustments.

Table 1: Hypothesized model adjustments predicted to give rise to the abnormal accommodative behavior seen in myopes. AC and CA cross-link strength were quantified as stimulus CA/C and response AC/A.

<table>
<thead>
<tr>
<th>Hypothesis</th>
<th>Prediction</th>
<th>Simulink parameter</th>
<th>Accommodative behavior (model predictions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Motor deficit (rigid plant)</td>
<td>Reduced plant gain</td>
<td>Plant gain</td>
<td>1. Increased accommodative lag.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Actual gain: 1.75</td>
<td>2. High AC/A and</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Altered gain: 1.25</td>
<td>accommodative adaptation.</td>
</tr>
<tr>
<td></td>
<td>Reduced fast controller gain</td>
<td>Fast controller</td>
<td>3. Reduced peak velocity and</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(phasic) gain</td>
<td>acceleration.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Actual gain: 2.5</td>
<td>4. Reduced CA/C</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Altered gain: 2.0,</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.5, 1.0</td>
<td></td>
</tr>
<tr>
<td>2) Sensory deficit (reduced blur sensitivity)</td>
<td>Large depth of focus (DOF)</td>
<td>Dead zone</td>
<td>1. Increased accommodative lag.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Actual DOF: ± 0.14</td>
<td>2. Unchanged AC/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Altered DOF: ±0.25</td>
<td>3. Reduced accommodative adaptation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.35</td>
<td>4. Reduced peak velocity and</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>acceleration.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5. Unchanged CA/C</td>
</tr>
<tr>
<td></td>
<td>Reduced accommodative sensory gain (ASG)</td>
<td>ASG gain</td>
<td>1. Increased accommodative lags.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Actual gain: 1</td>
<td>2. Unchanged AC/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Altered gain: 0.8,</td>
<td>3. Reduced adaptation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.6, and 0.4.</td>
<td>4. Reduced peak velocity and</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>acceleration.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5. Unchanged CA/C</td>
</tr>
<tr>
<td>3) Sensory motor interaction (altered feedback sensitivity)</td>
<td>Increased feedback gain</td>
<td>Feedback gain:</td>
<td>1. High response lags</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Actual gain: 1</td>
<td>2. Unchanged AC/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Altered gain: 1.2,</td>
<td>3. Unchanged CA/C</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.4 and 1.6</td>
<td>4. Reduced peak velocity and</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>acceleration.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5. Low accommodative adaptation</td>
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</tbody>
</table>
As shown in table 1, only simulation with a reduced accommodative plant gain predicted the abnormal behavior found in myopes. A rigid plant would also predict an altered main sequence (reduced rate of change of velocity and acceleration over response amplitude) coupled with a reduced accommodative response to both blur and disparity. To date there has been no measure of main sequence characteristics of the blur-driven accommodative responses in myopic children. While our group previously found no attenuation of convergence accommodation (CA) in children, they do point out that CA output might have been prolonged due to the decreased vergence adaptation found in the myopic children (Sreenivasan, Irving, & Bobier, 2014, 2012). Previous investigations tested accommodation to targets changing in depth where proximal and blur cues would be found together. Proximal cues would confound the isolation of a purely sensory or motor cause. Accommodative response was found to be different when stimulated using targets changing in depth compared to negative lenses (Gwiazda et al., 1993). It should be noted that negative lenses do not control image size, in fact, image size decreases with increasing stimulus levels which is actually opposite to the normal proximal cue. Measures of blur driven accommodation (BA) are typically achieved by using a simple Badal optical system where changes in the stimulus do not result in retinal image size changes (Atchison et al., 1995). One study looked at blur driven accommodative lags using a Badal system in children, however, they did not characterize the main sequence relationship (Mutti et al., 2006). The purpose of this investigation was to examine the hypothesis of a rigid accommodative plant explaining the abnormal behavior of accommodation in young myopes. Responses from myopes were compared to an age matched group of non myopes along with adults.

2 Methods:

2.1 Subject recruitment

12 school aged children, 6 myopes & 6 emmetropes (Age: 8-13 years), and 6 naive adults (Age: 21-35 years) were recruited from the clinic database at the School of Optometry and Vision Science, University of Waterloo. Informed consent for children was obtained from their parents after a verbal and a written explanation of the study. Consent was obtained directly from adult subjects. The study followed the tenets of Declaration of Helsinki and received ethical approval from the University of Waterloo office of research ethics review board.

Children were classified into two refractive groups based on their cycloplegic refraction. The myopic group (MYP) had equivalent spheres between –1.25D to -7.00D. Emmetropic children (EMM) had equivalent spheres between +0.50D to 0D. Adult group (ADT) had 4 stable myopes and 2 emmetropes. They were not subdivided based on refractive error given the evidence on similar accommodative dynamics between the stable adult myopes and emmetropes (Abott, Schmid, & Strang, 1998; Kasthurirangan & Glasser, 2005; Kasthurirangan, Vilupuru, & Glasser, 2003). Only subjects with no strabismus, no amblyopia, anisometropia < 1.00D, astigmatism < 1D and with best corrected visual acuity of 6/6 were included. All the myopes, both adults and children, were habitual soft contact lens wearers and wore their contact lenses during the study.
2.2 Instrumentation and Procedures

Data were collected over two visits, a screening visit to confirm the visual status of the subject and an experimental visit to measure the response dynamics to various accommodative stimuli. During the screening visit, baseline clinical measures including distance and near visual acuity, stereopsis, cycloplegic retinoscopy, and phoria (distance and near) measurement using cover test were performed on all the subjects.

2.2.1 Accommodative parameters

Experimental measures of gradient AC/A, accommodative adaptation and stimulus CA/C ratio were performed only on children using a Power-refractor (Multichannel systems, Germany). Calibration procedures followed for the PowerRefractor were similar to those described in previous studies (Sreenivasan, Irving, & Bobier, 2012, 2014). Gradient response AC/A (Accommodative convergence per diopter of accommodative response) was quantified as the change in the phoria with negative lenses. Modified Thorington technique was used to measure the phoria change and the procedure involved has been described in detail elsewhere (Sreenivasan, Irving, & Bobier, 2012). The child was then asked to watch an animated movie at 25cms for 20mins. Accommodative adaptation was measured as the difference in the resting focus before and after the near task. Resting focus was measured using a difference of Gaussian (DOG) target placed at 3m in a dark room with the left eye of the subject occluded. The peak spatial frequency present in the target was 0.18cpd. CA/C was quantified as the instant change in the accommodative response to known prisms when the child was fixating at the DOG placed at 3m. Stimuli ranging from $5\Delta$ - $15\Delta$ (5$\Delta$ steps) were placed in front of the left eye. A consensual change in the accommodation was measured from the right eye for 5s and then averaged.

2.2.2 Experimental design for measuring blur accommodation

The experimental visit followed the screening visit by not more than 10 days. A simple Badal optical system was used to present accommodative and disaccommodative stimuli. The subject was seated 1m away from the photorefractor with the left eye occluded. An IR passing mirror (Optical cast IR filter, Edmund Optics, USA) allowed an orthogonal presentation of the accommodative targets along with a continuous measure of accommodation using the dynamic photorefractor (see below). Two targets were manually placed at different distances from a +5D Badal lens. Each target was a high contrast (white on black) vertical line that was back illuminated using a white LED. A small horizontal offset was present between the two targets (maximum offset was 1.5° for a 3D stimulus). While the far target was always set at optical infinity, the near target was moved to various distances from the Badal lens to create various demands (1-3D, in 1D steps). Step stimuli were presented using a stimulus control tool box with a button that allowed for an instantaneous switch in the target distance. This switch was connected to an input-output control box that was further connected to the dynamic photorefraction system. This allowed a time stamp to be created when the target distance was switched. The order and presentation time of the step stimulus was varied to avoid predictability.

2.2.3 Dynamic photorefraction system (DPRS)

During the experimental visit, accommodation was measured using a custom built dynamic photorefractor (PROSILICA CAM (EC750), Allied Vision Technologies, Canada) that operated
at a sampling frequency of 70Hz, giving an output every 0.014 seconds. Photorefraction images were later analyzed offline (Suryakumar et al., 2009). The calibration protocol followed in this study for each subject was based on the procedures described previously (Schaeffel, Wilhelm, & Zrenner, 1993; Suryakumar et al., 2007). The DPRS was previously calibrated and validated on children and adults (Labhishetty, 2014).

### 2.2.4 Procedure

During the experimental visit, each subject was dilated using a drop of 2.5% Mydfrin (Phenylephrine hydrochloride) in both the eyes following an initial anterior chamber assessment. This optimized the photorefraction measures by ensuring a large pupil size (>4mm). The left eye of the subject was covered with an eye patch during the study to open the loop of the vergence system. The photorefractor was aligned to the right eye of the subject. Prior to the start of the study, 2-3 practice trials were given to each subject in order to familiarize them with the experimental procedures. Accommodative and disaccommodative step responses were recorded over 3 different stimulus amplitudes (1-3D in 1D steps). Six trials were conducted for each stimulus demand. Each trial lasted for approximately 5-10 seconds. The stimulus presentation time was controlled by the experimenter and was varied from 2-5 sec after the initiation of the trial to avoid prediction. Dynamic step responses were recorded for at least 3-5 sec after the presentation of the stimulus.

The order of stimulus presentation was randomized. Frequent breaks were given to the subject between the trials.

### 2.3 Data analysis

Final position traces (units of diopters) over time obtained from the DPRS were then loaded into MATLAB for further analysis. Velocity (diopters/s) and acceleration (diopters/s²) profiles were obtained by differentiating the response traces using a 2-point-difference algorithm. Position, velocity and acceleration traces were subsequently smoothed over a 100 msec window. The start and end of the response were identified using the velocity-criterion algorithm (Bharadwaj & Schor, 2005). The start of the response was the first data point on the position trace where the velocity exceeded 0.5 D/s and continued to do so for the next 100 msec. Similarly, the response was considered to be completed when the velocity fell below 90% of peak velocity and continued to do for the next 100ms. The start and the end points obtained using this criterion were later confirmed by visually inspecting each trace. An inverse of this criterion was used for the disaccommodative responses.

Deming regression and other statistical analysis were performed using GraphPad Prism (GraphPad Software Inc., USA) and STATISTICA (StatSoft, Inc., USA). For repeated measures ANOVA (Rm ANOVA), subject group (Myopes, emmetropes and adults) was considered as a between factor and stimulus amplitude (1D, 2D & 3D) as within factor.

### 3 Results

#### 3.1 Data distribution

Table 2: Distribution of various response patterns in accommodation and disaccommodation.

<table>
<thead>
<tr>
<th>Accommodation</th>
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<tbody>
<tr>
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</tbody>
</table>
Accommodation data were obtained from 12 children, 6 myopes (11.16 ± 1.00 years) & 6 emmetropes (11.16 ± 1.83 years), and 6 adults (26.16 ± 3.37 years). Given the cooperative nature of adults, each subject was tested at 3 stimulus levels with 6 trials for each target position for a total of 36 trials including both accommodation and disaccommodation. Given the off-line nature of the analysis, efforts were made to ensure that each subject provided at least 6 usable measures for each stimulus level. With children, response trials also involved head and eye movements, significantly larger number of blinks etc. which corrupt the data. Therefore, more trials (6-12 trials per stimulus demand) were performed on children to ensure that the required number of data trials were obtained from each child (table 2). As shown in table 2, measures were categorized into usable and unusable responses. The latter included measures with blinks, head movements and/or poor photorefractor image quality. Usable traces were further divided into Typical and Atypical responses (figure 2). Subjects showed a variety of atypical responses, broadly classified as Atypical I and II. Atypical I responses were classified into three types, (1) **Under-damped responses or dynamic overshoots**, where the responses showed overshoots before reaching the final steady state. (2) **Double step responses or dynamic undershoots**, where a second corrective response followed an initial undershoot. (3) **Multiple step responses**, where the final steady state was achieved after multiple error responses (fig 2(d)). Alternatively, Atypical II responses were classified into two types, (1) **Flat responses**, or responses that did not show a change in the steady state or responses that did not fit the velocity threshold criterion. These responses usually occurred with smaller stimulus demands. (2) **Ill sustained responses**, wherein the change in the accommodative response was not sustained. Atypical II responses were not used for further analysis. Dynamic analysis was performed on typical and atypical I responses separately. For the analysis of typical accommodative dynamics, the first 4 typical responses were considered. This allowed equal representation of the subjects’ responses in the final group results without any individual bias. Mean refractive error along with other critical visual parameters are provided in table 3.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Typical</th>
<th>Typical with blinks</th>
<th>Atypical I</th>
<th>Atypical II</th>
<th>Unusable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myopes (MYP)</td>
<td>55</td>
<td>7</td>
<td>30</td>
<td>15</td>
<td>28</td>
</tr>
<tr>
<td>Emmetropes (EMM)</td>
<td>49</td>
<td>5</td>
<td>25</td>
<td>16</td>
<td>21</td>
</tr>
<tr>
<td>Adults (ADT)</td>
<td>84</td>
<td>3</td>
<td>7</td>
<td>3</td>
<td>11</td>
</tr>
</tbody>
</table>

**Disaccommodation**

<table>
<thead>
<tr>
<th></th>
<th>MYP</th>
<th>EMM</th>
<th>ADT</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical</td>
<td>69</td>
<td>59</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>With</td>
<td>7</td>
<td>6</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Blinks</td>
<td>7</td>
<td>5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Atypical I</td>
<td>18</td>
<td>16</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>26</td>
<td>29</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Unusable</td>
<td></td>
<td></td>
<td></td>
<td>11</td>
</tr>
</tbody>
</table>
Typical responses were characterized by an initial exponential increase (accommodative) or decrease (disaccommodative) in the amplitude followed by a small asymptotic change to the final steady state (figure 2(a) & 3). A transient rise in the velocity corresponded to a change in the accommodative position. Latency (msec) was defined as the time taken for the initiation of the
response after the presentation of the stimulus and was ≈ 250 - 300 msec. Amplitude (Diopters) was defined as the dioptric difference between the start and end points. The time taken to reach the end point from the starting point was defined as the response time (msec). The maximum values in the velocity and acceleration traces were defined as the peak velocity (D/s) and peak acceleration (D/s²) respectively. “First order main sequence” relationship was obtained by plotting the peak velocities as a function of their respective response amplitudes. Similarly “Second order main sequence” relationship was defined by plotting peak acceleration as a function of the response amplitude. The time taken to reach the peak velocity value from 0 D/s is defined as the time to peak velocity (TPV in msec) and the total time taken for acceleration from 0D/s² to reach peak and decrease back to 0D/s² was defined as the total duration of acceleration (TDA in msec).

Historically the main sequence relationship has been analyzed using a univariate regression. However, given the variability noted in both the velocity/acceleration measures and response amplitudes, a bivariate regression would be more suitable. A bivariate analysis produced a better fit to the data (R squared) with significantly steeper slopes compared to a simple univariate analysis. Also, bivariate analysis did not influence any differences found between the groups (i.e. MYP vs EMM etc.) compared to that found using a simple linear regression. Therefore, bivariate regression (Deming regression) was used for analyzing the main sequence relationship for both accommodation and disaccommodation.

### 3.1.2 Atypical I responses

An atypical pattern was found in the responses where the steady state was reached but not in a smooth exponential manner as described above. These responses were categorized as atypical I responses. They were characterized by either an initial over or undershoot followed by a corrective response (figure 2(b, c & d)). Velocity and acceleration traces were characterized by two or more peaks that corresponded to erroneous and corrective response. Amplitude (Diopters) was defined as the dioptric difference between the start and end points for both initial and corrective responses. The start and end points were determined using the velocity threshold criterion as described previously. To measure the amount of over (figure 2b) or undershoot (figure 2c), an initial response was defined as the difference between the position at onset to the first local maximum that occurred before the initiation of a second response. A response differential for the corrective response was calculated as the difference between the initial erroneous position reached to the final steady state (Fukushima et al., 2009). The maximum values in the velocity and acceleration trace were defined as the peak velocity (D/s) and peak acceleration (D/s²) respectively. These parameters were defined separately for both erroneous and corrective responses. First and second order main sequence relationship for accommodation were compared between the typical and atypical I responses.

Since the number of atypical measures were unequal in the three groups (table 2), they were quantified based on their proportion, i.e. number of atypical responses over the total number of usable responses in each subject and group. For disaccommodation, there was a significant reduction in the frequency of atypical patterns in all the groups (table 2). Since there were fewer atypical disaccommodative responses (only double steps), further analysis was not performed. The
Impact of refractive error, age and stimulus demand on the frequency of atypical I responses was also tested for accommodation.

Table 3: Critical visual parameters of myopic and emmetropic children

<table>
<thead>
<tr>
<th>Parameter</th>
<th>EMM</th>
<th>MYP</th>
<th>ADT</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>11.16 ± 1.83</td>
<td>11.16 ± 1.0</td>
<td>26.5 ± 3.56</td>
<td>-</td>
</tr>
<tr>
<td>Refractive error (D)</td>
<td>0 ± 0.25D</td>
<td>-3.7 ± 2.0</td>
<td>-1.91 ± 1.61</td>
<td>-</td>
</tr>
<tr>
<td>Near phoria (Δ) (-ve: exo; +ve: eso)</td>
<td>-1.83 ± 2.13</td>
<td>1 ± 3.57</td>
<td>-0.83 ± 0.98</td>
<td>-</td>
</tr>
<tr>
<td>Stimulus AC/A ratio (Δ/D)</td>
<td>4.00 ± 0.63</td>
<td>4.50 ± 0.50</td>
<td>-</td>
<td>0.17</td>
</tr>
<tr>
<td>Response AC/A ratio (Δ/D)</td>
<td>4.16 ± 0.57</td>
<td>6.66 ± 1.09</td>
<td>-</td>
<td>0.005</td>
</tr>
<tr>
<td>Stimulus CA/C ratio (D/Δ)</td>
<td>0.07 ± 0.009</td>
<td>0.05 ± 0.006</td>
<td>-</td>
<td>0.29</td>
</tr>
<tr>
<td>Accommodative adaptation (D)</td>
<td>0.08 ± 0.04</td>
<td>0.25 ± 0.05</td>
<td>-</td>
<td>0.0001</td>
</tr>
</tbody>
</table>
3.2 Typical responses

Figure 3: Typical accommodative and disaccommodative traces for a 3D stimulus demand. Group averaged accommodative and disaccommodative position (3a, 3d), velocity (3b, 3e) and acceleration (3c, 3f) traces were plotted as a function of time. (3a, 3d) The data were normalized from different observers in each group before averaging. When the stimulus was presented at 0 sec, the initiation of the response occurred after ≈ 250 - 300 msec. Total time taken to complete the response was about a second. Velocity and acceleration (D/s²) traces were obtained by differentiating the position traces.
3.2.1 Dynamic characteristics of accommodation and disaccommodation

3.2.1.1 Temporal parameters

(Figure 4: Latency and response time of accommodation and disaccommodation across the three groups and stimulus demands. The error bars indicate the standard deviation. Asterisk symbols indicate the level of significance (** – p < 0.05)

Figure 4 shows the mean latency and response time exhibited by subjects in the three groups for both accommodation (a, b) and disaccommodation (c, d). For accommodation (ACC), repeated measures ANOVA (Rm ANOVA) showed that the latency was not significantly different between the three groups (F (2, 15) = 1.22, p = 0.32) and stimulus demands (F (2, 30) = 1.00, p = 0.37). However, for disaccommodation (DACC), latency was significantly different between the three groups (F (2, 15) = 12.39, p < 0.001) but not across the stimulus demands (F (2, 30) = 2.38, p = 0.10). Post hoc (Tukey HSD) analysis showed that ADT exhibited significantly longer latencies compared to the EMM across all the stimulus demands (p < 0.05). For both ACC and DACC, the response time was significantly different between the three stimulus amplitudes (ACC: F (2, 30) = 12.37, p < 0.001; DACC: F (2, 30) = 32.99, p < 0.0001) but not across the three groups (ACC: F (2, 15) = 1.44, p = 0.27; DACC: F (2, 15) = 1.11, p = 0.35). Post hoc Tukey suggested that the response time was significantly smaller for a 1D stimulus compared to the larger demands across all the groups (p < 0.05).
3.2.1.2 Response amplitude

For both ACC and DACC, repeated measures ANOVA showed that the response amplitude was significantly different between the three groups (ACC: F (2, 15) = 29.0, p < 0.0001; DACC: F (2, 15) = 37.7, p < 0.001) and between stimulus demands (ACC: F (2, 30) = 355.30, p < 0.0001; DACC: F (2, 30) = 659.80, p < 0.0001). Further, a significant interaction was noted between the groups and stimulus demands (ACC: F (4, 30) = 5.20, p < 0.0001; DACC: F (4, 30) = 8.1, p < 0.001). As shown in figure 5, post hoc analysis showed that MYP exhibited significantly reduced response amplitudes compared to other groups for demands larger than 1D (p < 0.01) of both accommodation and disaccommodation.

3.2.1.3 Velocity and acceleration dynamics

Figure 6 (a, b) shows the velocity main sequence (MS) of the three groups. The slopes of the velocity MS for all the groups were significantly different from a zero slope (p < 0.0001). For ACC, although the slopes of the MS were not significantly different between the MYP vs EMM (F (1, 91) = 0.06, p = 0.79) and MYP vs ADT (F (1, 124) = 1.86, p = 0.17), a statistically significant difference in the slope of MS was noted between the EMM vs ADT (F (1, 121) = 4.15, p = 0.04). Also, the intercept of MS was significantly different between MYP and ADT (F (1, 125) = 4.16; p = 0.04). For DACC, the slopes of the MS were not significantly different between the MYP vs EMM (F (1, 102) = 0.14, p = 0.70), MYP vs ADT (F (1, 123) = 0.01, p = 0.89), and EMM vs ADT (F (1, 123) = 0.14, p = 0.70). However, the intercept of MS was significantly different between the EMM vs ADT (F (1, 124) = 11.74; p = 0.0008) and MYP vs ADT (F (1, 124) = 10.02; p = 0.001).
Figure 6: Main sequence characteristics of accommodation and disaccommodation. (a, b) Peak velocity was plotted as a function of the response amplitude for both accommodation and disaccommodation. (b, d) Time to peak velocity was plotted as a function of response amplitude. (e, f) Peak acceleration was plotted as a function of the response amplitude for both accommodation and disaccommodation. (g, h) Total duration of acceleration was plotted as a function of response amplitude. As indicated in the picture, red circles indicate data from myopes, green circle from adults and blue squares indicate emmetropes. Solid lines represent deming regression fits. Given the variance in both x and y variables of the main sequence plot, a simple linear regression was not used. P values indicate the level of difference of the MS slopes from a zero slope.

Time to peak velocity (TPV) was also compared across the three groups for accommodation and disaccommodation (figure 6 (c, d)). The slopes of the TPV over the response amplitudes were not significantly different from zero ($p > 0.05$). No significant difference was noted in the slope of TPV between MYP vs EMM (ACC: $F (1, 91) = 0.45, p = 0.50$; DACC: $F (1, 102) = 0.63, p = 0.42$), MYP vs ADT (ACC: $F (1, 124) = 0.009, p = 0.92$; DACC: $F (1, 123) = 0.78, p = 0.37$) and EMM vs ADT (ACC: $F (1, 121) = 0.58; p = 0.44$; DACC: $F (1, 123) = 0.01; p = 0.91$). However, for DACC, the intercept of the TPV was significantly different between EMM and ADT ($F (1, 124) = 9.48; p = 0.002$).

Figure 6 (e, f) represents the acceleration main sequence of the three groups. The slopes of the acceleration MS for all the groups were significantly different from a zero slope ($p < 0.05$). The slopes of the MS were not significantly different between the MYP vs EMM (ACC: $F (1, 91) = 0.0004, p = 0.98$; DACC: $F (1, 102) = 0.002, p = 0.95$) and MYP vs ADT (ACC: $F (1, 124) = 1.60, p = 0.20$; DACC: $F (1, 123) = 0.77, p = 0.37$), and EMM vs ADT (ACC: $F (1, 121) = 2.19, p = 0.14$; DACC: $F (1, 123) = 1.44, p = 0.23$). But the intercept of MS was significantly different between the MYP vs ADT (ACC: $F (1, 125) = 8.06, p = 0.005$; DACC: $F (1, 124) = 30.56; p < 0.0001$), and EMM vs ADT (ACC: $F (1, 122) = 22.13; p < 0.0001$; DACC: $F (1, 124) = 37.24, p < 0.0001$). Total duration of acceleration (TDA) was also compared across the three groups (Figure 6 (g, h)). For accommodation, the slopes of the TDA over the response amplitudes were significantly different from zero ($p < 0.01$) except for MYP ($p > 0.05$). For disaccommodation, the slopes of the TDA over the response amplitudes were significantly different from zero all the three groups ($p < 0.05$). No significant difference was noted in the slope of TDA between MYP vs EMM (ACC: $F (1, 91) = 1.11, p = 0.29$; DACC: $F (1, 102) = 0.002, p = 0.95$), MYP vs ADT (ACC: $F (1, 124) = 0.86, p = 0.34$; DACC: $F (1, 123) = 0.29, p = 0.58$) and EMM vs ADT (ACC: $F (1, 121) = 0.10; p = 0.74$; DACC: $F (1, 123) = 0.42; p = 0.51$).

### 3.3 Atypical I responses

Response integrals for double step accommodative responses and dynamic overshoots ranged from $0.28D - 1.46D$ ($0.78D ± 0.35D$) and $0.2D - 1.15D$ ($0.42D ± 0.21D$) respectively. Rm ANOVA was used to compare the response patterns between the three groups and the three stimulus amplitudes. While the frequency of the useable responses were not different ($F (2, 15) = 1.59; p = 0.23$), the frequency of other response patterns was significantly different ($F (3, 45) = 141.17, p < 0.0001$) between the groups. Post hoc Tukey suggested no significant difference in the frequency of atypical responses between MYP and EMM ($p > 0.05$). However, a significant difference was noted in the frequency of atypical responses between children and adults ($p < 0.05$). The frequency of response patterns was also significantly different ($F (3, 153) = 81.30; p < 0.0001$) between the three stimulus amplitudes. Post hoc (Tukey) suggested that atypical II i.e. flat and ill-sustained responses occurred more with 1D compared to 2 and 3D stimulus ($p < 0.05$). Furthermore, no
individual bias was noted within the three groups (MYP: F (5, 12) = 0.79; p = 0.57; EMM: F (5, 12) = 1.60; p = 0.23); ADT: F (5, 12) = 1.85; p = 0.17).

3.3.1 Main sequence characteristics

Figure 7: Velocity and acceleration main sequence of atypical accommodative responses. Peak velocity (a, c, e) and peak acceleration (b, d, f) were plotted as a function of the response amplitude for myopic children (a, b), emmetropic children (c, d) and adults (e, f). While the red squares in the picture indicate atypical responses, blue circles indicate data from the typical responses. The solid lines indicate the deming regression fits. Overall, no significant difference was noted in the main sequence slopes between typical and atypical responses (p>0.1).
Velocity and acceleration main sequence (MS) were compared between the typical and atypical responses in children and adults (figure 7). For the MS analysis, both initial and corrective pulses were considered. The slopes of the velocity main sequence were not significantly different between the typical and atypical responses in all the groups (MYP: \( p = 0.25 \); EMM: \( p = 0.23 \); ADT: \( p = 0.13 \)). Similarly, the slopes of the acceleration main sequence were not significantly different in all the groups (MYP: \( p = 0.38 \); EMM: \( p = 0.89 \); ADT: \( p = 0.53 \)).

4 Discussion

Blur driven accommodation was successfully recorded from all the three groups. In agreement with previous studies, our typical response data showed that myopic children exhibit significantly larger response lags that increase with demand (Mutti et al., 2006). However, myopic children showed a main sequence relationship similar to the emmetropes. Other dynamic characteristics such as latency, response time etc. were not different between the two refractive groups for both accommodation and disaccommodation. Adults showed an overall reduction in the response dynamics such as peak velocity and acceleration compared to children. The present investigation also confirms the previous findings of high response AC/A, high accommodative adaptation and unchanged CA/C (Gwiazda et al., 1995b, 2005; Sreenivasan, Irving & Bobier, 2014). Atypical accommodative responses were consistently found in the children with and without myopia. While atypical II responses suggest varying levels of attention, others (atypical I) may reflect a developmental pattern of the motor system.

4.1 Accommodative mechanism and myopia

A reduced accommodative plant gain would explain the pattern of high lags of accommodation coupled with an elevated response AC/A and high accommodative adaptation. However, it failed to explain the findings of similar disparity accommodation (CA/C) and MS relationship compared to emmetropes. Also, given the transient nature of the abnormal accommodation, it would be difficult to imagine a plant deficit that could be temporary (Abott, Schmid & Strang, 1998; Gwiazda et al., 1995a). A sensory deficit modelled as either a large DOF or reduced ASG would predict the patterns of reduced blur accommodation, unchanged MS relationship and CA/C. However, it would not predict the abnormal pattern of high response AC/A and high adaptation. Previously, studies have suggested that the abnormal behavior of accommodation may be due to an increased effort to accommodate given the remote accommodative resting state in corrected MYPs compared to EMMs (Ebenholtz & Zander, 1987; Gwiazda et al., 1995b). An increased effort to accommodate should elevate both stimulus as well as response AC/A. However, consistent with the previous investigation, we found a similar stimulus AC/A between myopic and non-myopic children (Mutti et al., 2000). This suggests that the resulting accommodative convergence for a given target distance remains constant even with a reduced accommodative response. This might suggest an increase in the AC cross-link gain to compensate for reduced accommodation.

We provide a novel model simulation (Table 4) which does predict the empirical evidence. This was achieved by including an elevated AC cross-link gain, a reduced tonic vergence controller and a reduced ASG. Based on the simulations, we propose that the reduced blur sensitivity (ASG) seen in the myopic children is compensated by a motor recalibration wherein the gain of the
accommodative convergence crosslink is increased. A larger gain of the crosslink would be necessary to maintain sufficient levels of vergence given the reduced accommodation. The capacity to increase AC gain is consistent with past studies on adults (Bobier & McRae, 1996; Jiang & Ramamirtham, 2005; Judge, 1987; Miles, Judge, & Optican, 1987). We recognize that gains in AC/A linkage are more difficult to change in adults compared to the adaptive system gains. However, since the direction of such adjustments appear to be necessary for children undergoing increases in inter-pupillary distance (IPD) with age, perhaps this adjustment is more plastic at a younger age (MacLachlan & Howland, 2002). The transient nature of this recalibration in the AC gain could be in the response to the reduced blur sensitivity which improves when myopia stabilizes. The increase in accommodative adaptation was modelled by reducing the gain of vergence adaptation in myopes (Sreenivasan, Irving, & Bobier, 2012, 2014). A stronger tonic accommodative controller may also be necessary to turn off the high AC cross-link and avoid esophoria with sustained viewing (Schor & Kotulak, 1986).

Table 4: Myopia prediction model

<table>
<thead>
<tr>
<th>Hypothesis</th>
<th>Prediction and Simulink parameter</th>
<th>Agreement with empirical evidence</th>
<th>Disagreement with empirical evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor (AC/A) adjustment to compensate for reduced ASG</td>
<td><strong>Reduced ASG</strong>&lt;br&gt;Actual gain: 1&lt;br&gt;Altered gain: 0.8, 0.6, 0.4</td>
<td>1. High response lags&lt;br&gt;2. High accommodative adaptation</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td><strong>High AC gain</strong>&lt;br&gt;Actual gain: 0.65&lt;br&gt;Altered gain: 0.7, 0.85, 1.15</td>
<td>3. High response AC/A&lt;br&gt;4. Unchanged stimulus AC</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Reduced tonic vergence gain</strong>&lt;br&gt;Actual gain: 1.5&lt;br&gt;Altered: 1.2, 1.0</td>
<td>5. Unchanged stimulus CA/C&lt;br&gt;6. Unchanged main sequence</td>
<td></td>
</tr>
</tbody>
</table>

4.2 Dynamic characteristics in adults

Dynamic characteristics of accommodation and disaccommodation have been extensively studied on adults (Bharadwaj & Schor, 2005, 2006; Campbell & Westheimer, 1960; Kasthurirangan & Glasser, 2005b; Schaeffel, Wilhelm, & Zrenner, 1993; Suryakumar et al., 2007). Data on the temporal characteristics (such as latency, response amplitude, TPV and TDA) and velocity MS relationship found in our subjects were in agreement with the previous investigations (Bharadwaj & Schor, 2006; Bharadwaj & Schor, 2005; Suryakumar et al., 2007). Previous investigation found that accommodative acceleration was independent of the response amplitude (Bharadwaj & Schor, 2005). However, a positive acceleration MS was noted in all our subject groups (both typical and atypical). Given that both the studies had a similar age range of subjects and measured blur only accommodation, this discrepancy cannot be explained. This positive MS relationship noted in our study would imply that similar to other motor systems such as vergence, accommodative pulse innervation might proportionally increase with the response amplitude. Furthermore, our results also confirm an age related trend in main sequence relationship for both accommodation and disaccommodation (Schor & Bharadwaj, 2005).
4.3 Atypical I responses

Atypical patterns were previously found in saccades and vergence. Studies on adults showed atypical patterns such as the dynamic overshoots and oscillations in saccades (Bahill, Clark, & Stark, 1975; Bahill, Hsu, & Stark, 1978; Doslak, Dell’osso, & Daroff, 1983; Zee, Robinson, & Eng, 1979). These atypical patterns were predicted to be due to either an unstable (Zee, Robinson, & Eng, 1979) or an inaccurate pulse generator (Bahill et al., 1975). Also, atypical patterns like the double step responses found here were shown to exist with the vergence system (Alvarez et al., 2000; Semmlow et al., 1994). They predicted that these patterns occur due to an inaccurate response initiation like the saccades.

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Figure 8: Modelling of an underdamped pulse-step response to a 1D step stimulus where an open loop, pre-programmed pulse is followed by a closed loop step (visually guided). A typical response would occur when the pulse and step output accurately match the input. Based on our data, we predict that an atypical response occurs due to an inaccurate pulse innervation. Accommodative response (solid black line) along with (a) acceleration and (b) velocity (dotted gray line) were plotted as a function of time. An excessive initial pulse output (indicated by dashed red box) leads to an overshoot in the response. The error would be detected by the internal feedback of the step system. This would initiate a corrective response (shown in the solid blue box) to reach the final steady state.

Our results are in agreement with the current models where accommodation is characterized by a preprogrammed pulse system along with a visually guided step system. Given the similar main sequence relationship between the typical and atypical I patterns, an initial inaccurate pulse might explain the over or undershoots. The visually guided step system might then detect this error and initiate a corrective pulse to reach the final steady state. Studies on accommodation under stereoscopic conditions have suggested that atypical patterns occur due to an excessive CA output that constitutes the initial part of the response under binocular viewing conditions (Fukushima et al., 2009; Torii et al., 2008). However, our data shows that atypical response patterns do exist with blur only accommodation. We speculate that these atypical patterns of accommodation might occur due to an inaccurate pulse initiation and cannot be purely explained based on the system that drives the response (Figure 8). Previous investigation also found significantly larger proportion of atypical accommodative responses in their younger subjects (3-5 years old) compared to the older ones. However, they did not quantify or categorize these atypical patterns other than to separate them from normal responses (Anderson et al., 2010). We suspect that the atypical response patterns in children could be part of a calibration process in the internal feedback system to respond quickly.
and accurately to varying accommodative stimuli. The lack of atypical responses in disaccommodation in our study might be due to the fact that all the responses were directed close to the resting levels of accommodation (Bharadwaj & Schor, 2006).

5 Conclusion

Results from the present study conclude that the abnormal behavior of accommodation in myopic school children couldn’t be explained by a purely motor or sensory model. Based on the current understanding of the accommodation, a reduced blur sensitivity coupled with a motor recalibration of the AC cross-link predicts this transient but consistent behavior seen in progressive myopes.

6 Acknowledgements

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7 References


