

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.

1 Introduction

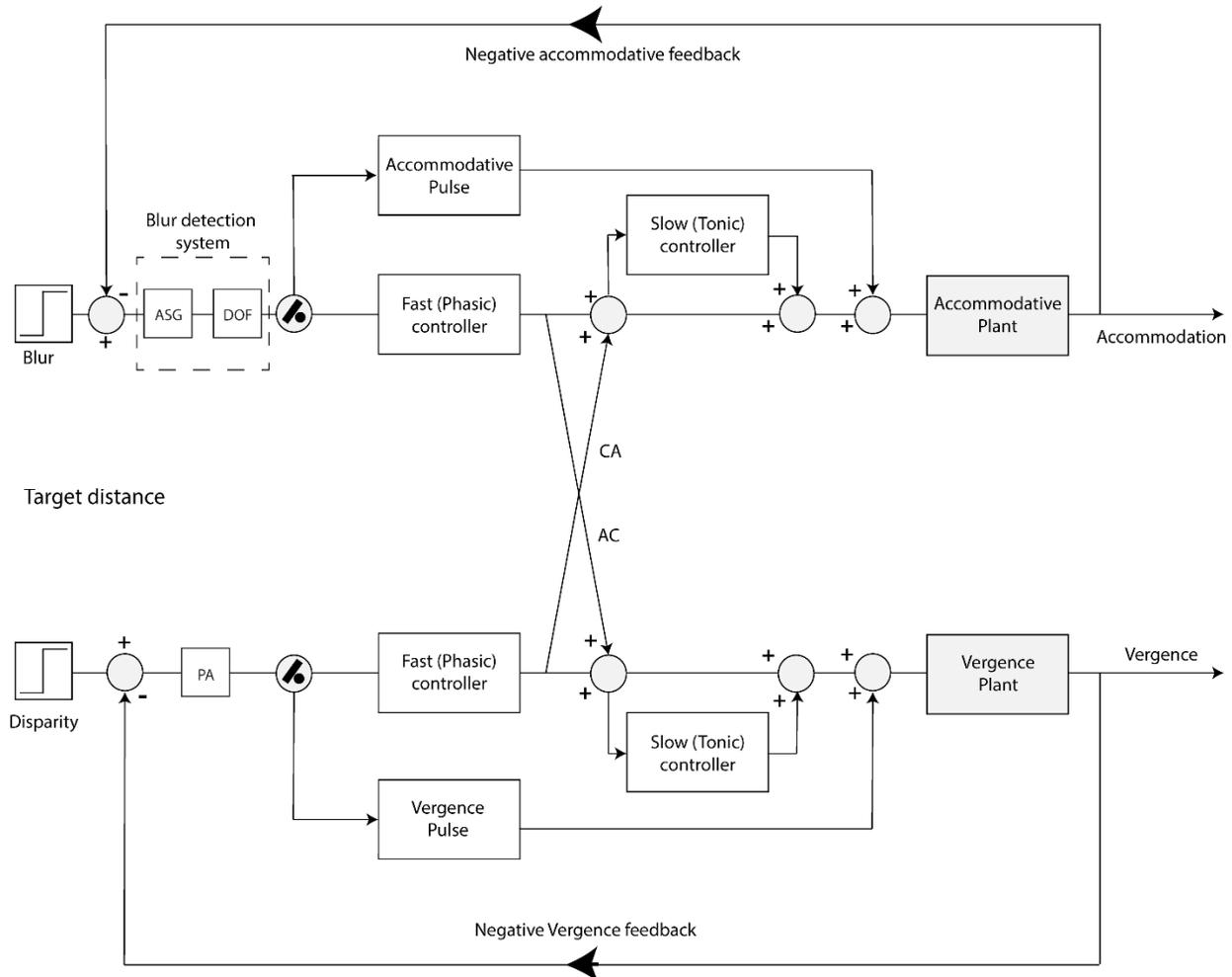
2 Progressive myopes exhibit an accommodative behavior characterized by high response lags that
3 increase with the demand (Gwiazda et al., 1995a; Gwiazda et al., 1993; Koomson et al., 2015;
4 Mutti et al., 2006; Nakatsuka et al., 2005), elevated response AC/A (Gwiazda, Grice, & Thorn,
5 1999; Gwiazda, Thorn, & Held, 2005; Mutti et al., 2000), and high accommodative adaptation
6 (Gwiazda et al., 1995b; Sreenivasan, Irving, & Bobier, 2012). These patterns are not predicted by
7 the currently accepted models of accommodation and vergence which suggest that a high
8 accommodative adaptation would be associated with a low AC/A and smaller response lags (Schor
9 & Bharadwaj, 2006; Schor, 1992). Myopes also show high steady state fluctuations (Langaas et
10 al., 2008; Sreenivasan, Irving, & Bobier, 2011), reduced vergence adaptation (Sreenivasan, Irving
11 & Bobier, 2012) and a large depth of focus (Rosenfield & Abraham-Cohen, 1999; Vasudevan,
12 Ciuffreda, & Wang, 2006). Furthermore, several studies showed that the onset of myopia is
13 associated with changes in the accommodative response (Gwiazda et al., 2005; Mutti et al., 2006).
14 Interestingly, this abnormal behavior is associated only with progressive and not stable myopia
15 (Abott, Schmid, & Strang, 1998; Gwiazda et al., 1995a; Jiang & Morse, 1999). Nevertheless, these
16 patterns of accommodation do not appear to be causative because correction of the lags does not
17 reduce the myopic progression to a significant clinical level (Berntsen et al., 2012; Gwiazda et al.,
18 2004; Shapiro, Kelly, & Howland, 2005).

19 Studies on children and adults have found differences in the accommodative plant of myopes,
20 specifically, altered crystalline lens growth (Goss et al., 1997; Jones et al., 2005; Mutti et al., 2012,
21 2000, 1998; Philip et al., 2014; Shih, Chiang, & Lin, 2009; Zadnik et al., 1995) along with a thick
22 and rigid ciliary muscle (Bailey, Sinnott, & Mutti, 2008; Buckhurst et al., 2013; Jeon et al., 2012;
23 Lewis et al., 2012; Lossing et al., 2012; Oliveira et al., 2005; Pucker et al., 2013). Previous work
24 showed that the equatorial growth of the crystalline lens ceases earlier in myopes compared to the
25 non-myopes (Mutti et al., 1998). They predicted that the failure of the lens to compensate for the
26 axial growth of the eye could lead to an increased tension on the choroid and hinder
27 accommodation. However, no study to date has shown if these anatomical differences would
28 actually lead to an abnormal accommodative behavior. A recent investigation (Gwiazda et al.,
29 2015) found no correlation between myopia progression and changes in the lens growth pattern.
30 They concluded that changes in the lens thickness do not accompany or cause myopia and could
31 be merely coincidental.

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

44 ASG predicted increased response lags as the stimulus demand increased, similar to the empirical
45 accommodative measures.

46 1.1 Model simulations



47
48 **Figure 1: Model of accommodation and vergence adapted for myopes (Adapted from Schor, 1992; Jiang, 1997, Maxwell et**
49 **al., 2010). The control mechanism of accommodation and vergence is characterized by a pulse step innervation. For**
50 **accommodation, response to a step stimulus is initiated by an open-loop pulse followed by a closed loop step system that**
51 **code for the dynamic characteristics and position respectively. The closed loop step system is predicted to be under the**
52 **influence of an internal feedback to avoid errors in the response. The interactions between accommodation and vergence**
53 **are characterized by pulse and step cross-link. For simplicity, we have not shown the internal feedback and the pulse cross-**
54 **link mechanism. The cross-links CA and AC are approximated empirically using measures of CA/C and AC/A respectively**
55 **and are represented as gains in the model. We also adapted the ASG (Jiang, 1997) into this model to address the blur**
56 **detection system of accommodation. DOF: Depth of focus; PA: Panum's area and ASG: Accommodative sensory gain.**

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

63 predict the abnormal accommodative behavior. Table 1 below lists the outcomes of the model
 64 adjustments.

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

Hypothesis	Prediction	Simulink parameter	Accommodative behavior (model predictions)
1) Motor deficit (rigid plant)	Reduced plant gain	Plant gain Actual gain: 1.75 Altered gain: 1.25, 0.75	1. Increased accommodative lag. 2. High AC/A and accommodative adaptation. 3. Reduced peak velocity and acceleration. 4. Reduced CA/C
	Reduced fast controller gain	Fast controller (phasic) gain Actual gain: 2.5 Altered gain: 2.0, 1.5, 1.0	1. Increased accommodative lag. 2. Unchanged AC/A 3. Reduced accommodative adaptation 4. Unchanged CA/C 5. Reduced peak velocity and acceleration
2) Sensory deficit (reduced blur sensitivity)	Large depth of focus (DOF)	Dead zone Actual DOF: ± 0.14 Altered DOF: $\pm 0.25, 0.35$	1. Increased accommodative lag. 2. Unchanged AC/A 3. Reduced accommodative adaptation 4. Reduced peak velocity and acceleration. 5. Unchanged CA/C
	Reduced accommodative sensory gain (ASG)	ASG gain Actual gain: 1 Altered gain: 0.8, 0.6, and 0.4.	1. Increased accommodative lags. 2. Unchanged AC/A 3. Reduced adaptation 4. Reduced peak velocity and acceleration. 5. Unchanged CA/C
3) Sensory motor interaction (altered feedback sensitivity)	Increased feedback gain	Feedback gain: Actual gain: 1 Altered gain: 1.2, 1.4 and 1.6	1. High response lags 2. Unchanged AC/A 3. Unchanged CA/C 4. Reduced peak velocity and acceleration. 5. Low accommodative adaptation

67 As shown in table 1, only simulation with a reduced accommodative plant gain predicted the
68 abnormal behavior found in myopes. A rigid plant would also predict an altered main sequence
69 (reduced rate of change of velocity and acceleration over response amplitude) coupled with a
70 reduced accommodative response to both blur and disparity. To date there has been no measure of
71 main sequence characteristics of the blur-driven accommodative responses in myopic children.
72 While our group previously found no attenuation of convergence accommodation (CA) in children,
73 they do point out that CA output might have been prolonged due to the decreased vergence
74 adaptation found in the myopic children (Sreenivasan, Irving, & Bobier, 2014, 2012). Previous
75 investigations tested accommodation to targets changing in depth where proximal and blur cues
76 would be found together. Proximal cues would confound the isolation of a purely sensory or motor
77 cause. Accommodative response was found to be different when stimulated using targets changing
78 in depth compared to negative lenses (Gwiazda et al., 1993). It should be noted that negative lenses
79 do not control image size, in fact, image size decreases with increasing stimulus levels which is
80 actually opposite to the normal proximal cue. Measures of blur driven accommodation (BA) are
81 typically achieved by using a simple Badal optical system where changes in the stimulus do not
82 result in retinal image size changes (Atchison et al., 1995). One study looked at blur driven
83 accommodative lags using a Badal system in children, however, they did not characterize the main
84 sequence relationship (Mutti et al., 2006). The purpose of this investigation was to examine the
85 hypothesis of a rigid accommodative plant explaining the abnormal behavior of accommodation
86 in young myopes. Responses from myopes were compared to an age matched group of non myopes
87 along with adults.

88 **2 Methods:**

89 **2.1 Subject recruitment**

90 12 school aged children, 6 myopes & 6 emmetropes (Age: 8-13 years), and 6 naive adults (Age:
91 21-35 years) were recruited from the clinic database at the School of Optometry and Vision
92 Science, University of Waterloo. Informed consent for children was obtained from their parents
93 after a verbal and a written explanation of the study. Consent was obtained directly from adult
94 subjects. The study followed the tenets of Declaration of Helsinki and received ethical approval
95 from the University of Waterloo office of research ethics review board.

96 Children were classified into two refractive groups based on their cycloplegic refraction. The
97 myopic group (MYP) had equivalent spheres between -1.25D to -7.00D . Emmetropic children
98 (EMM) had equivalent spheres between $+0.50\text{D}$ to 0D . Adult group (ADT) had 4 stable myopes
99 and 2 emmetropes. They were not subdivided based on refractive error given the evidence on
100 similar accommodative dynamics between the stable adult myopes and emmetropes (Abott,
101 Schmid, & Strang, 1998; Kasthurirangan & Glasser, 2005; Kasthurirangan, Vilupuru, & Glasser,
102 2003). Only subjects with no strabismus, no amblyopia, anisometropia $< 1.00\text{D}$, astigmatism $< 1\text{D}$
103 and with best corrected visual acuity of 6/6 were included. All the myopes, both adults and
104 children, were habitual soft contact lens wearers and wore their contact lenses during the study.

105 **2.2 Instrumentation and Procedures**

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

111 **2.2.1 Accommodative parameters**

112 Experimental measures of gradient AC/A, accommodative adaptation and stimulus CA/C ratio
113 were performed only on children using a Power-refractor (Multichannel systems, Germany).
114 Calibration procedures followed for the PowerRefractor were similar to those described in
115 previous studies (Sreenivasan, Irving, & Bobier, 2012, 2014). Gradient response AC/A
116 (Accommodative convergence per diopter of accommodative response) was quantified as the
117 change in the phoria with negative lenses. Modified Thorington technique was used to measure
118 the phoria change and the procedure involved has been described in detail elsewhere (Sreenivasan,
119 Irving, & Bobier, 2012). The child was then asked to watch an animated movie at 25cms for
120 20mins. Accommodative adaptation was measured as the difference in the resting focus before
121 and after the near task. Resting focus was measured using a difference of Gaussian (DOG) target
122 placed at 3m in a dark room with the left eye of the subject occluded. The peak spatial frequency
123 present in the target was 0.18cpd. CA/C was quantified as the instant change in the accommodative
124 response to known prisms when the child was fixating at the DOG placed at 3m. Stimuli ranging
125 from 5Δ - 15Δ (5Δ steps) were placed in front of the left eye. A consensual change in the
126 accommodation was measured from the right eye for 5s and then averaged.

127 **2.2.2 Experimental design for measuring blur accommodation**

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

143 **2.2.3 Dynamic photorefraction system (DPRS)**

144 During the experimental visit, accommodation was measured using a custom built dynamic
145 photorefractor (PROSILICA CAM (EC750), Allied Vision Technologies, Canada) that operated

146 at a sampling frequency of 70Hz, giving an output every 0.014 seconds. Photorefractive images
147 were later analyzed offline (Suryakumar et al., 2009). The calibration protocol followed in this
148 study for each subject was based on the procedures described previously (Schaeffel, Wilhelm, &
149 Zrenner, 1993; Suryakumar et al., 2007). The DPRS was previously calibrated and validated on
150 children and adults (Labhishetty, 2014).

151 **2.2.4 Procedure**

152 During the experimental visit, each subject was dilated using a drop of 2.5% Mydrin
153 (Phenylephrine hydrochloride) in both the eyes following an initial anterior chamber assessment.
154 This optimized the photorefractive measures by ensuring a large pupil size (>4mm). The left eye
155 of the subject was covered with an eye patch during the study to open the loop of the vergence
156 system. The photorefractor was aligned to the right eye of the subject. Prior to the start of the study,
157 2-3 practice trials were given to each subject in order to familiarize them with the experimental
158 procedures. Accommodative and disaccommodative step responses were recorded over 3 different
159 stimulus amplitudes (1-3D in 1D steps). Six trials were conducted for each stimulus demand. Each
160 trial lasted for approximately 5-10 seconds. The stimulus presentation time was controlled by the
161 experimenter and was varied from 2-5 sec after the initiation of the trial to avoid prediction.
162 Dynamic step responses were recorded for at least 3-5 sec after the presentation of the stimulus.
163 The order of stimulus presentation was randomized. Frequent breaks were given to the subject
164 between the trials.

165 **2.3 Data analysis**

166 Final position traces (units of diopters) over time obtained from the DPRS were then loaded into
167 MATLAB for further analysis. Velocity (diopters/s) and acceleration (diopters/s²) profiles were
168 obtained by differentiating the response traces using a 2-point-difference algorithm. Position,
169 velocity and acceleration traces were subsequently smoothed over a 100 msec window. The start
170 and end of the response were identified using the velocity-criterion algorithm (Bharadwaj & Schor,
171 2005). The start of the response was the first data point on the position trace where the velocity
172 exceeded 0.5 D/s and continued to do so for the next 100 msec. Similarly, the response was
173 considered to be completed when the velocity fell below 90% of peak velocity and continued to
174 do for the next 100ms. The start and the end points obtained using this criterion were later
175 confirmed by visually inspecting each trace. An inverse of this criterion was used for the
176 disaccommodative responses.

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

181 **3 Results**

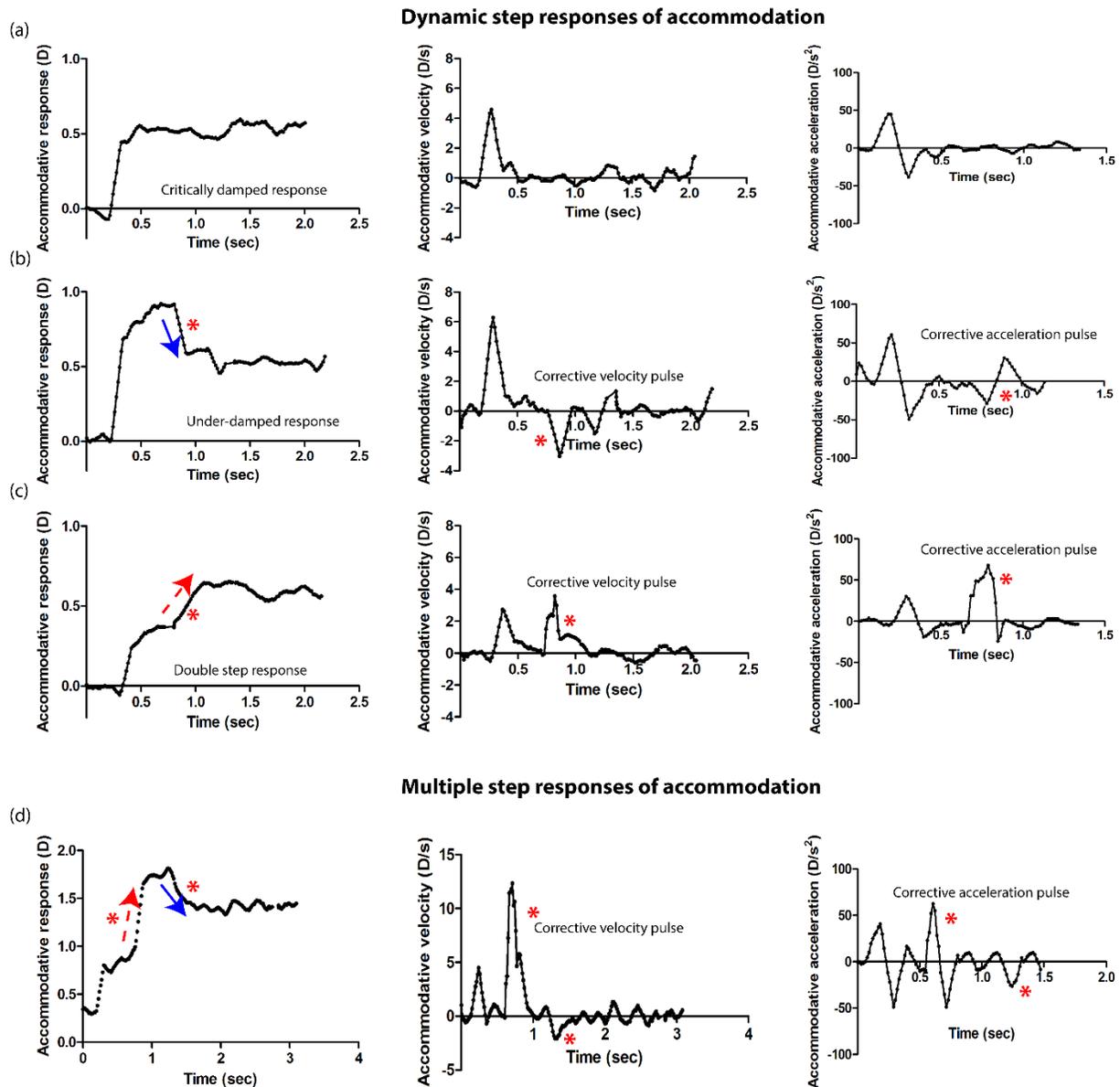
182 **3.1 Data distribution**

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

Accommodation

<i>Groups</i>	<i>Typical</i>	<i>Typical with blinks</i>	<i>Atypical I</i>	<i>Atypical II</i>	<i>Unusable</i>
Myopes (MYP)	55	7	30	15	28
Emmetropes (EMM)	49	5	25	16	21
Adults (ADT)	84	3	7	3	11
Disaccommodation					
MYP	69	7	7	18	26
EMM	59	6	5	16	29
ADT	80	6	1	5	16

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



210

211 **Figure 2: Individual representative typical and atypical accommodative response traces to a step stimulus.**

212 (a) A typical (critically damped) accommodative response to a 1D stimulus is accompanied by the resulting velocity and
 213 acceleration traces. The system achieved the steady state without any oscillations. (b) An atypical underdamped response
 214 shows an initial dynamic overshoot that occurred due to an inaccurate acceleration and velocity pulse followed by a
 215 corrective response (*). Similarly (c) represents a double step (undershoots) response. An initial undershoot is followed by
 216 a corrective response in the same direction to reach the final steady state. (d) Multiple step response to a 2D stimulus from
 217 the same subject. An initial undershoot is followed by an over compensated second response requiring a third corrective
 218 response to reach the final steady state.

219 3.1.1 Typical responses

220 Typical responses were characterized by an initial exponential increase (accommodative) or
 221 decrease (disaccommodative) in the amplitude followed by a small asymptotic change to the final
 222 steady state (figure 2(a) & 3). A transient rise in the velocity corresponded to a change in the
 223 accommodative position. Latency (msec) was defined as the time taken for the initiation of the

224 response after the presentation of the stimulus and was $\approx 250 - 300$ msec. Amplitude (Diopters)
225 was defined as the dioptric difference between the start and end points. The time taken to reach
226 the end point from the starting point was defined as the response time (msec). The maximum values
227 in the velocity and acceleration traces were defined as the peak velocity (D/s) and peak acceleration
228 (D/s^2) respectively. “First order main sequence” relationship was obtained by plotting the peak
229 velocities as a function of their respective response amplitudes. Similarly “Second order main
230 sequence” relationship was defined by plotting peak acceleration as a function of the response
231 amplitude. The time taken to reach the peak velocity value from 0 D/s is defined as the time to
232 peak velocity (TPV in msec) and the total time taken for acceleration from $0D/s^2$ to reach peak and
233 decrease back to $0D/s^2$ was defined as the total duration of acceleration (TDA in msec).
234 Historically the main sequence relationship has been analyzed using a univariate regression.
235 However, given the variability noted in both the velocity/acceleration measures and response
236 amplitudes, a bivariate regression would be more suitable. A bivariate analysis produced a better
237 fit to the data (R squared) with significantly steeper slopes compared to a simple univariate
238 analysis. Also, bivariate analysis did not influence any differences found between the groups (i.e.
239 MYP vs EMM etc.) compared to that found using a simple linear regression. Therefore, bivariate
240 regression (Deming regression) was used for analyzing the main sequence relationship for both
241 accommodation and disaccommodation.

242 **3.1.2 Atypical I responses**

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

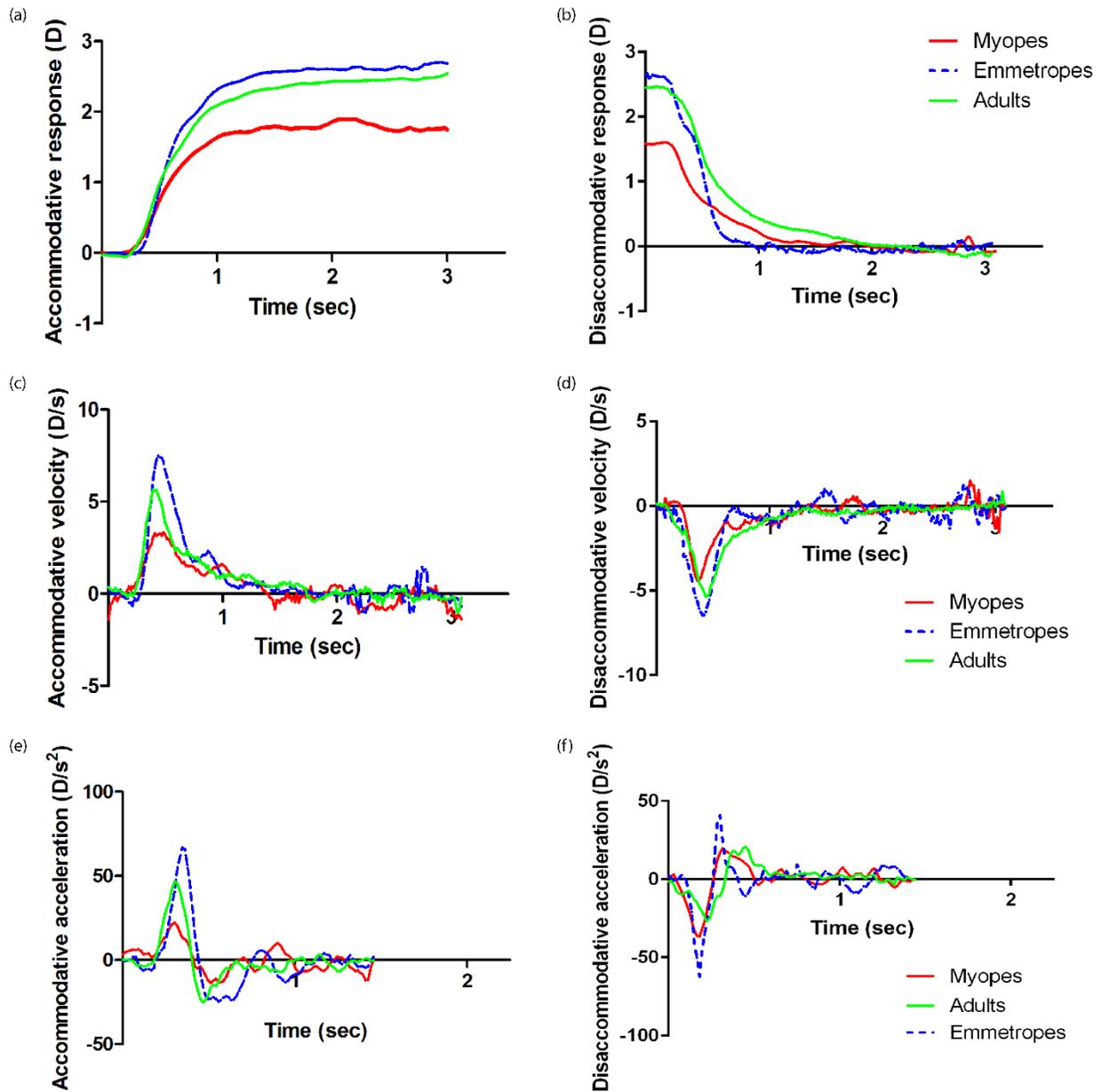
259 Since the number of atypical measures were unequal in the three groups (table 2), they were
260 quantified based on their proportion, i.e. number of atypical responses over the total number of
261 usable responses in each subject and group. For disaccommodation, there was a significant
262 reduction in the frequency of atypical patterns in all the groups (table 2). Since there were fewer
263 atypical disaccommodative responses (only double steps), further analysis was not performed. The

264 impact of refractive error, age and stimulus demand on the frequency of atypical I responses was
265 also tested for accommodation.

266 **Table 3: Critical visual parameters of myopic and emmetropic children**

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

267 3.2 Typical responses



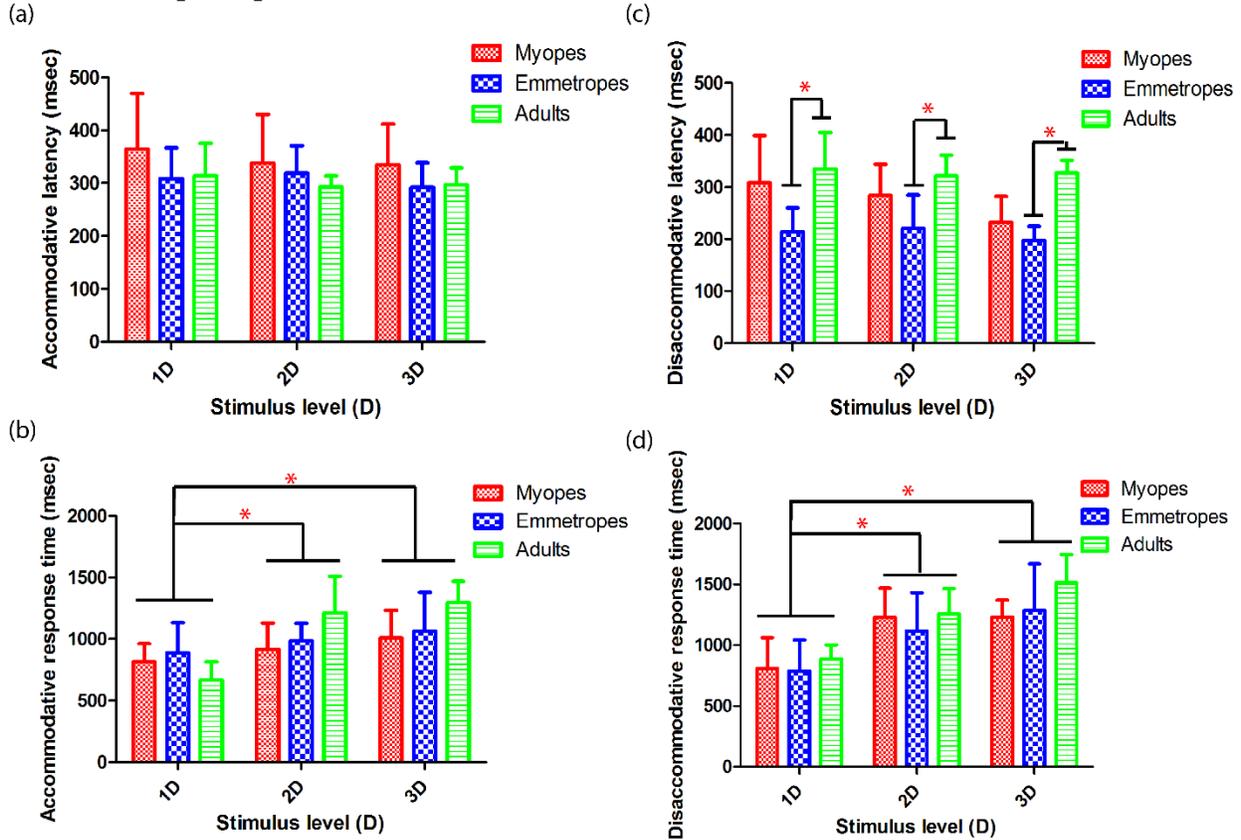
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Figure 3: Typical accommodative and disaccommodative traces for a 3D stimulus demand. Group averaged accommodative and disaccommodative position (3a, 3d), velocity (3b, 3e) and acceleration (3c, 3f) traces were plotted as a function of time. (3a, 3d) 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 $\approx 250 - 300$ 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.

274 **3.2.1 Dynamic characteristics of accommodation and disaccommodation**

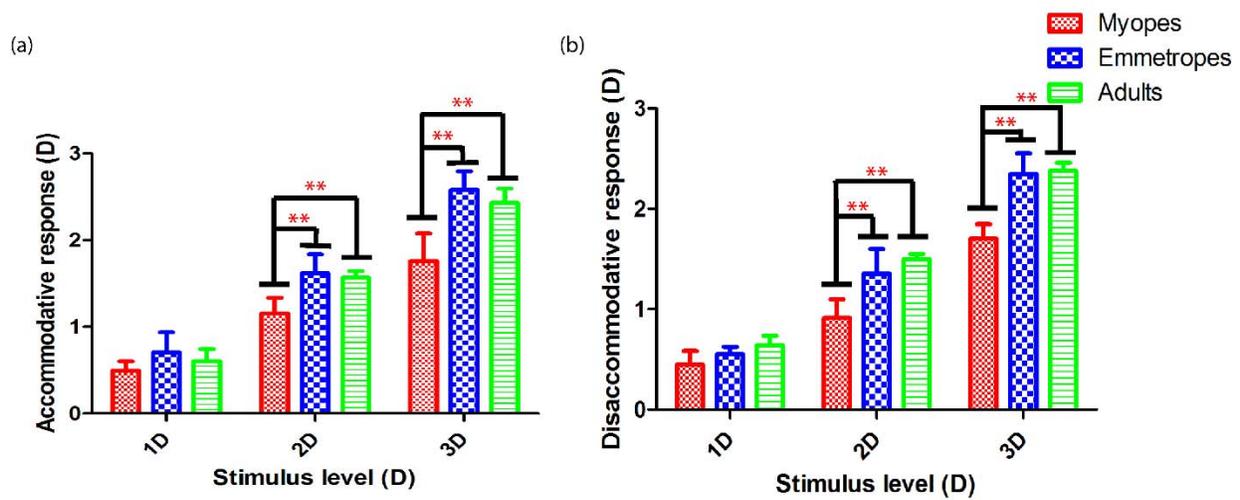
275 **3.2.1.1 Temporal parameters**



276
277 **Figure 4: Latency and response time of accommodation and disaccommodation across the three groups and stimulus**
278 **demands. The errors bars indicate the standard deviation. Asterisk symbols indicate the level of significance (** – p < 0.05)**

279 Figure 4 shows the mean latency and response time exhibited by subjects in the three groups for
280 both accommodation (a, b) and disaccommodation (c, d). For accommodation (**ACC**), repeated
281 measures ANOVA (Rm ANOVA) showed that the latency was not significantly different between
282 the three groups ($F(2, 15) = 1.22, p = 0.32$) and stimulus demands ($F(2, 30) = 1.00, p = 0.37$).
283 However, for disaccommodation (**DACC**), latency was significantly different between the three
284 groups ($F(2, 15) = 12.39, p < 0.001$) but not across the stimulus demands ($F(2, 30) = 2.38, p =$
285 0.10). Post hoc (Tukey HSD) analysis showed that ADT exhibited significantly longer latencies
286 compared to the EMM across all the stimulus demands ($p < 0.05$). For both ACC and DACC, the
287 response time was significantly different between the three stimulus amplitudes (ACC: $F(2, 30)$
288 $= 12.37, p < 0.001$; DACC: $F(2, 30) = 32.99, p < 0.0001$) but not across the three groups (ACC:
289 $F(2, 15) = 1.44, p = 0.27$; DACC: $F(2, 15) = 1.11, p = 0.35$). Post hoc Tukey suggested that the
290 response time was significantly smaller for a 1D stimulus compared to the larger demands across
291 all the groups ($p < 0.05$).

292 **3.2.1.2 Response amplitude**



293

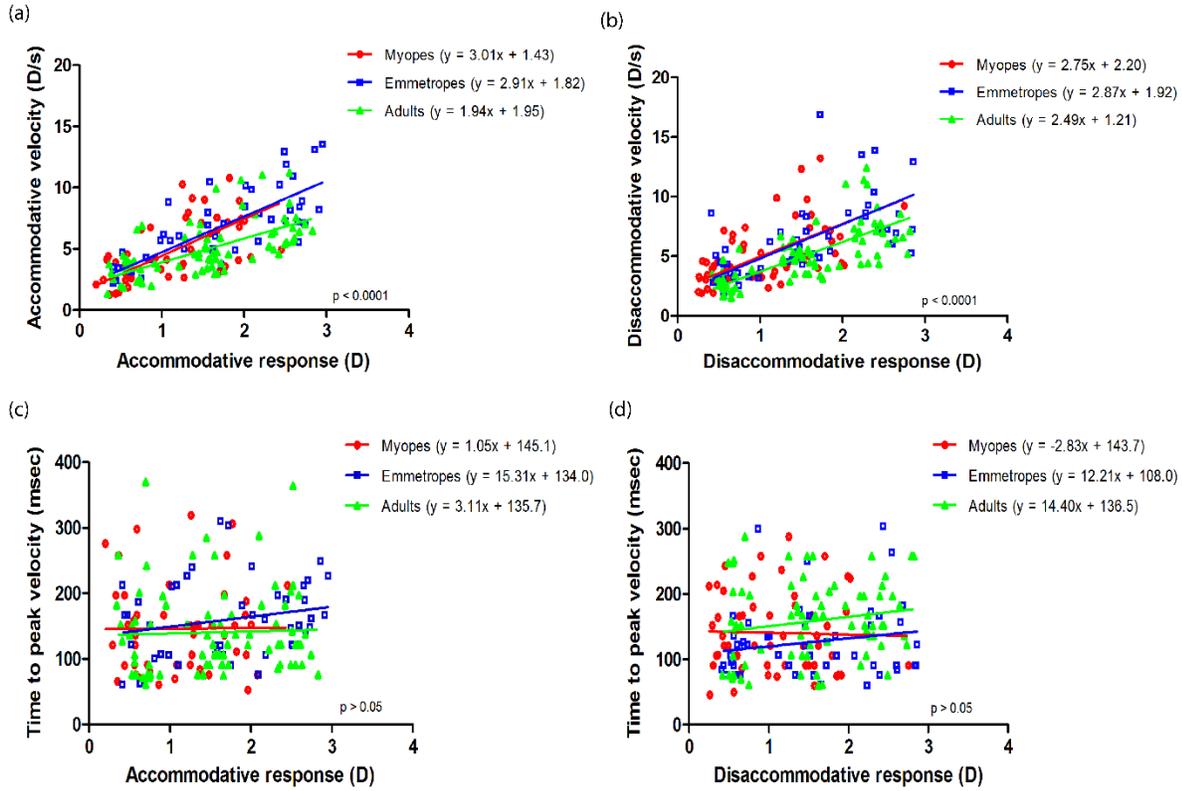
294 **Figure 5: Response amplitude of accommodation and disaccommodation in relation to the stimulus demand across the three**
 295 **groups. Error bars indicate the standard deviation. Asterisk symbols indicate the level of significance (***) – $p < 0.01$**

296 For both ACC and DACC, repeated measures ANOVA showed that the response amplitude was
 297 significantly different between the three groups (ACC: $F(2, 15) = 29.0, p < 0.0001$; DACC: $F(2,$
 298 $15) = 37.7, p < 0.001$) and between stimulus demands (ACC: $F(2, 30) = 355.30, p < 0.0001$;
 299 DACC: $F(2, 30) = 659.80, p < 0.0001$). Further, a significant interaction was noted between the
 300 groups and stimulus demands (ACC: $F(4, 30) = 5.20, p = 0.003$; DACC: $F(4, 30) = 8.1, p <$
 301 0.001). As shown in figure 5, post hoc analysis showed that MYP exhibited significantly reduced
 302 response amplitudes compared to other groups for demands larger than 1D ($p < 0.01$) of both
 303 accommodation and disaccommodation.

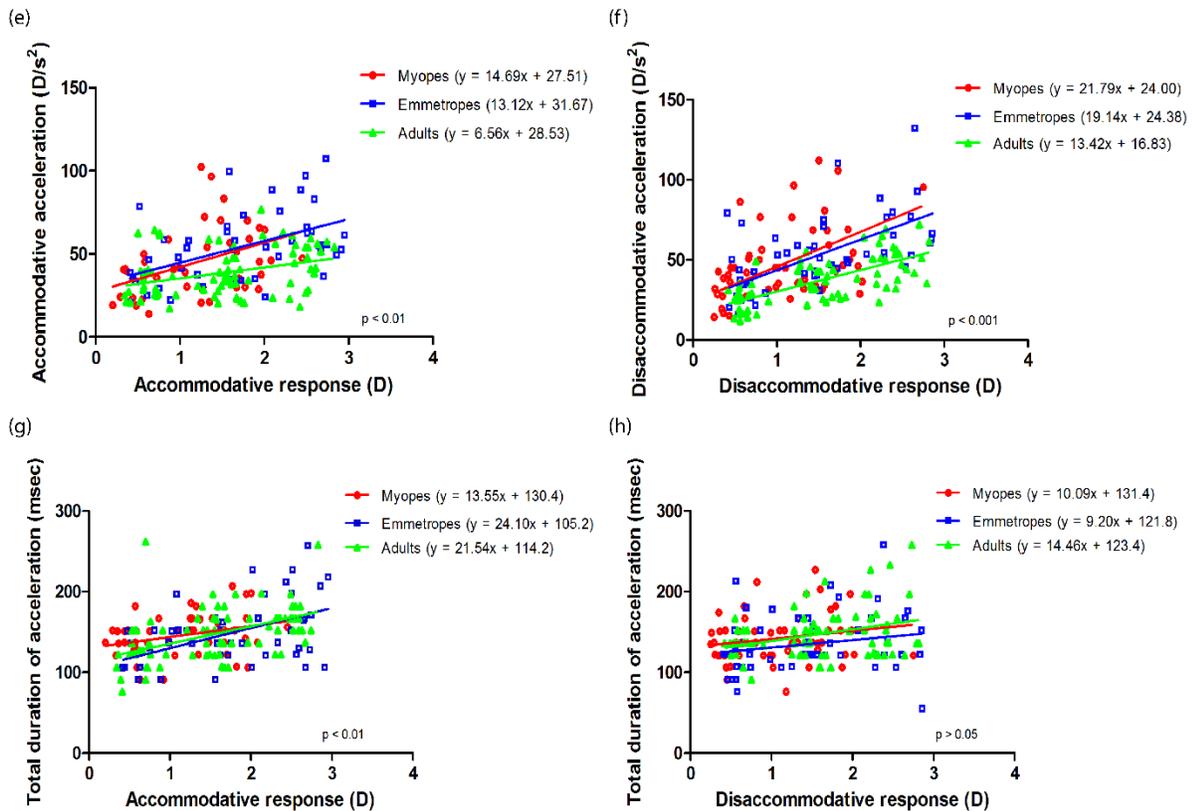
304 **3.2.1.3 Velocity and acceleration dynamics**

305 Figure 6 (a, b) shows the velocity main sequence (MS) of the three groups. The slopes of the
 306 velocity MS for all the groups were significantly different from a zero slope ($p < 0.0001$). For
 307 ACC, although the slopes of the MS were not significantly different between the MYP vs EMM
 308 ($F(1, 91) = 0.06, p = 0.79$) and MYP vs ADT ($F(1, 124) = 1.86, p = 0.17$), a statistically significant
 309 difference in the slope of MS was noted between the EMM vs ADT ($F(1, 121) = 4.15, p = 0.04$).
 310 Also, the intercept of MS was significantly different between MYP and ADT ($F(1, 125) = 4.16$;
 311 $p = 0.04$). For DACC, the slopes of the MS were not significantly different between the MYP vs
 312 EMM ($F(1, 102) = 0.14, p = 0.70$), MYP vs ADT ($F(1, 123) = 0.01, p = 0.89$), and EMM vs ADT
 313 ($F(1, 123) = 0.14, p = 0.70$). However, the intercept of MS was significantly different between the
 314 EMM vs ADT ($F(1, 124) = 11.74; p = 0.0008$) and MYP vs ADT ($F(1, 124) = 10.02; p = 0.001$).

Velocity main sequence



Acceleration main sequence



316 **Figure 6: Main sequence characteristics of accommodation and disaccommodation. (a, b) Peak velocity was plotted as a**
317 **function of the response amplitude for both accommodation and disaccommodation. (b, d) Time to peak velocity was plotted**
318 **as a function of response amplitude. (e, f) Peak acceleration was plotted as a function of the response amplitude for both**
319 **accommodation and disaccommodation. (g, h) Total duration of acceleration was plotted as a function of response**
320 **amplitude. As indicated in the picture, red circles indicate data from myopes, green circle from adults and blue squares**
321 **indicate emmetropes. Solid lines represent deming regression fits. Given the variance in both x and y variables of the main**
322 **sequence plot, a simple linear regression was not used. P values indicate the level of difference of the MS slopes from a zero**
323 **slope.**

324 Time to peak velocity (TPV) was also compared across the three groups for accommodation and
325 disaccommodation (figure 6 (c, d)). The slopes of the TPV over the response amplitudes were not
326 significantly different from zero ($p > 0.05$). No significant difference was noted in the slope of
327 TPV between MYP vs EMM (ACC: $F(1, 91) = 0.45$, $p = 0.50$; DACC: $F(1, 102) = 0.63$, $p =$
328 0.42), MYP vs ADT (ACC: $F(1, 124) = 0.009$, $p = 0.92$; DACC: $F(1, 123) = 0.78$, $p = 0.37$) and
329 EMM vs ADT (ACC: $F(1, 121) = 0.58$; $p = 0.44$; DACC: $F(1, 123) = 0.01$; $p = 0.91$). However,
330 for DACC, the intercept of the TPV was significantly different between EMM and ADT ($F(1,$
331 $124) = 9.48$; $p = 0.002$).

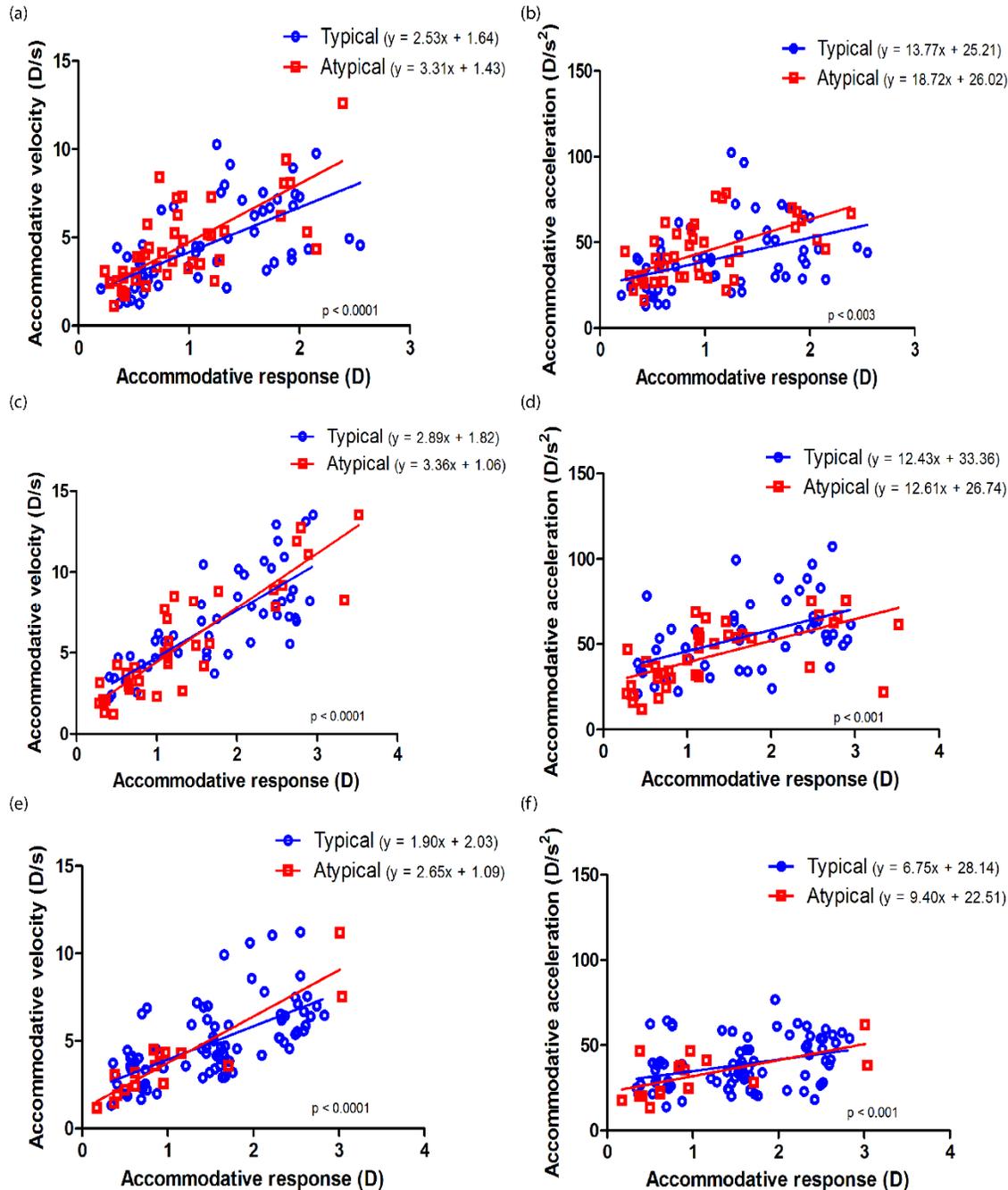
332 Figure 6 (e, f) represents the acceleration main sequence of the three groups. The slopes of the
333 acceleration MS for all the groups were significantly different from a zero slope ($p < 0.05$). The
334 slopes of the MS were not significantly different between the MYP vs EMM (ACC: $F(1, 91) =$
335 0.0004 , $p = 0.98$; DACC: $F(1, 102) = 0.002$, $p = 0.95$) and MYP vs ADT (ACC: $F(1, 124) = 1.60$,
336 $p = 0.20$; DACC: $F(1, 123) = 0.77$, $p = 0.37$), and EMM vs ADT (ACC: $F(1, 121) = 2.19$, $p =$
337 0.14 ; DACC: $F(1, 123) = 1.44$, $p = 0.23$). But the intercept of MS was significantly different
338 between the MYP vs ADT (ACC: $F(1, 125) = 8.06$, $p = 0.005$; DACC: $F(1, 124) = 30.56$; $p <$
339 0.0001), and EMM vs ADT (ACC: $F(1, 122) = 22.13$; $p < 0.0001$; DACC: $F(1, 124) = 37.24$, p
340 < 0.0001). Total duration of acceleration (TDA) was also compared across the three groups (Figure
341 6 (g, h)). For accommodation, the slopes of the TDA over the response amplitudes were
342 significantly different from zero ($p < 0.01$) except for MYP ($p > 0.05$). For disaccommodation, the
343 slopes of the TDA over the response amplitudes were significantly different from zero all the three
344 groups ($p < 0.05$). No significant difference was noted in the slope of TDA between MYP vs EMM
345 (ACC: $F(1, 91) = 1.11$, $p = 0.29$; DACC: $F(1, 102) = 0.002$, $p = 0.95$), MYP vs ADT (ACC: $F(1,$
346 $124) = 0.86$, $p = 0.34$; DACC: $F(1, 123) = 0.29$, $p = 0.58$) and EMM vs ADT (ACC: $F(1, 121) =$
347 0.10 ; $p = 0.74$; DACC: $F(1, 123) = 0.42$; $p = 0.51$).

348 **3.3 Atypical I responses**

349 Response integrals for double step accommodative responses and dynamic overshoots ranged from
350 $0.28D - 1.46D$ ($0.78D \pm 0.35D$) and $0.2D - 1.15D$ ($0.42D \pm 0.21D$) respectively. Rm ANOVA
351 was used to compare the response patterns between the three groups and the three stimulus
352 amplitudes. While the frequency of the useable responses were not different ($F(2, 15) = 1.59$; $p =$
353 0.23), the frequency of other response patterns was significantly different ($F(3, 45) = 141.17$, $p <$
354 0.0001) between the groups. Post hoc Tukey suggested no significant difference in the frequency
355 of atypical responses between MYP and EMM ($p > 0.05$). However, a significant difference was
356 noted in the frequency of atypical responses between children and adults ($p < 0.05$). The frequency
357 of response patterns was also significantly different ($F(3, 153) = 81.30$; $p < 0.0001$) between the
358 three stimulus amplitudes. Post hoc (Tukey) suggested that atypical II i.e. flat and ill-sustained
359 responses occurred more with 1D compared to 2 and 3D stimulus ($p < 0.05$). Furthermore, no

360 individual bias was noted within the three groups (MYP: $F(5, 12) = 0.79$; $p = 0.57$; EMM: $F(5,$
 361 $12) = 1.60$; $p = 0.23$; ADT: $F(5, 12) = 1.85$; $p = 0.17$).

362 **3.3.1 Main sequence characteristics**



363
 364 **Figure 7: Velocity and acceleration main sequence of atypical accommodative responses. Peak velocity (a, c, e) and peak**
 365 **acceleration (b, d, f) were plotted as a function of the response amplitude for myopic children (a, b), emmetropic children**
 366 **(c, d) and adults (e, f). While the red squares in the picture indicate atypical responses, blue circles indicate data from the**
 367 **typical responses. The solid lines indicate the deming regression fits. Overall, no significant difference was noted in the main**
 368 **sequence slopes between typical and atypical responses ($p > 0.1$).**

369 Velocity and acceleration main sequence (MS) were compared between the typical and atypical
370 responses in children and adults (figure 7). For the MS analysis, both initial and corrective pulses
371 were considered. The slopes of the velocity main sequence were not significantly different between
372 the typical and atypical responses in all the groups (MYP: $p = 0.25$; EMM: $p = 0.23$; ADT: $p =$
373 0.13). Similarly, the slopes of the acceleration main sequence were not significantly different in
374 all the groups (MYP: $p = 0.38$; EMM: $p = 0.89$; ADT: $p = 0.53$).

375 **4 Discussion**

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

388 **4.1 Accommodative mechanism and myopia**

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

406 We provide a novel model simulation (Table 4) which does predict the empirical evidence. This
407 was achieved by including an elevated AC cross-link gain, a reduced tonic vergence controller and
408 a reduced ASG. Based on the simulations, we propose that the reduced blur sensitivity (ASG) seen
409 in the myopic children is compensated by a motor recalibration wherein the gain of the

410 accommodative convergence crosslink is increased. A larger gain of the crosslink would be
 411 necessary to maintain sufficient levels of vergence given the reduced accommodation. The
 412 capacity to increase AC gain is consistent with past studies on adults (Bobier & McRae, 1996;
 413 Jiang & Ramamirtham, 2005; Judge, 1987; Miles, Judge, & Optican, 1987). We recognize that
 414 gains in AC/A linkage are more difficult to change in adults compared to the adaptive system
 415 gains. However, since the direction of such adjustments appear to be necessary for children
 416 undergoing increases in inter-pupillary distance (IPD) with age, perhaps this adjustment is more
 417 plastic at a younger age (MacLachlan & Howland, 2002). The transient nature of this recalibration
 418 in the AC gain could be in the response to the reduced blur sensitivity which improves when
 419 myopia stabilizes. The increase in accommodative adaptation was modelled by reducing the gain
 420 of vergence adaptation in myopes (Sreenivasan, Irving, & Bobier, 2012, 2014). A stronger tonic
 421 accommodative controller may also be necessary to turn off the high AC cross-link and avoid
 422 esophoria with sustained viewing (Schor & Kotulak, 1986).

423 **Table 4: Myopia prediction model**

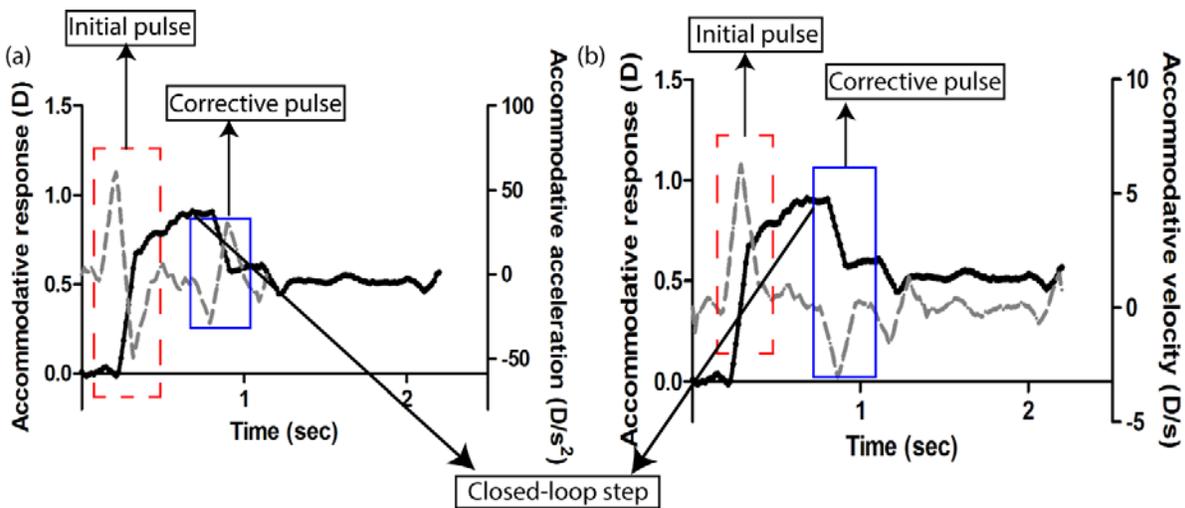
Hypothesis	Prediction and Simulink parameter	Agreement with empirical evidence	Disagreement with empirical evidence
Motor (AC/A) adjustment to compensate for reduced ASG	Reduced ASG	1. High response lags	None
	Actual gain: 1	2. High accommodative adaptation	
	Altered gain: 0.8, 0.6, 0.4	3. High response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

424 **4.2 Dynamic characteristics in adults**

425 Dynamic characteristics of accommodation and disaccommodation have been extensively studied
 426 on adults (Bharadwaj & Schor, 2005, 2006; Campbell & Westheimer, 1960; Kasthurirangan &
 427 Glasser, 2005b; Schaeffel, Wilhelm, & Zrenner, 1993; Suryakumar et al., 2007). Data on the
 428 temporal characteristics (such as latency, response amplitude, TPV and TDA) and velocity MS
 429 relationship found in our subjects were in agreement with the previous investigations (Bharadwaj
 430 & Schor, 2006; Bharadwaj & Schor, 2005; Suryakumar et al., 2007). Previous investigation found
 431 that accommodative acceleration was independent of the response amplitude (Bharadwaj & Schor,
 432 2005). However, a positive acceleration MS was noted in all our subject groups (both typical and
 433 atypical). Given that both the studies had a similar age range of subjects and measured blur only
 434 accommodation, this discrepancy cannot be explained. This positive MS relationship noted in our
 435 study would imply that similar to other motor systems such as vergence, accommodative pulse
 436 innervation might proportionally increase with the response amplitude. Furthermore, our results
 437 also confirm an age related trend in main sequence relationship for both accommodation and
 438 disaccommodation (Schor & Bharadwaj, 2005).

439 **4.3 Atypical I responses**

440 Atypical patterns were previously found in saccades and vergence. Studies on adults showed
441 atypical patterns such as the dynamic overshoots and oscillations in saccades (Bahill, Clark, &
442 Stark, 1975; Bahill, Hsu, & Stark, 1978; Doslak, Dell’osso, & Daroff, 1983; Zee, Robinson, &
443 Eng, 1979). These atypical patterns were predicted to be due to either an unstable (Zee, Robinson,
444 & Eng, 1979) or an inaccurate pulse generator (Bahill et al., 1975). Also, atypical patterns like the
445 double step responses found here were shown to exist with the vergence system (Alvarez et al.,
446 2000; Semmlow et al., 1994). They predicted that these patterns occur due to an inaccurate
447 response initiation like the saccades.



448
449 **Figure 8: Modelling of an underdamped pulse-step response to a 1D step stimulus where an open loop, pre-programmed**
450 **pulse is followed by a closed loop step (visually guided). A typical response would occur when the pulse and step output**
451 **accurately match the input. Based on our data, we predict that an atypical response occurs due to an inaccurate pulse**
452 **innervation. Accommodative response (solid black line) along with (a) acceleration and (b) velocity (dotted gray line) were**
453 **plotted as a function of time. An excessive initial pulse output (indicated by dashed red box) leads to an overshoot in the**
454 **response. The error would be detected by the internal feedback of the step system. This would initiate a corrective response**
455 **(shown in the solid blue box) to reach the final steady state.**

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

471 and accurately to varying accommodative stimuli. The lack of atypical responses in
472 disaccommodation in our study might be due to the fact that all the responses were directed close
473 to the resting levels of accommodation (Bharadwaj & Schor, 2006).

474 **5 Conclusion**

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

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