Longitudinal Evaluation of Accommodation During Treatment for Unilateral Amblyopia

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PURPOSE. Retinal image quality is dependent on accommodative performance. This longitudinal observational study of children with unilateral amblyopia evaluated the accommodative performance of the amblyopic eye during treatment.

METHODS. Twenty-six participants with unilateral amblyopia and 10 participants with typical vision aged 3 to 10 years participated. Accommodative response was measured using modified Nott retinoscopy in monocular and binocular viewing conditions for target distances of 50, 33, and 25 cm, at enrollment and each follow-up visit.

RESULTS. Participants with amblyopia accommodated less accurately when viewing with their amblyopic eye in monocular than in binocular conditions. Over the course of amblyopia treatment, accommodative performance improved with amblyopic eye visual acuity (VA) improvement, although this was not consistent across individual participants. A linear mixed model showed that accommodative error worsened with increasing depth of amblyopia for monocular viewing with the amblyopic eye (0.14 diopter [D] per line of acuity loss, $P = 0.001$), with an interaction between VA and stimulus demand (0.09 D of additional lag per diopter of stimulus, per line of acuity loss, $P < 0.001$). Participant age, patching duration, length of time in the study, history of strabismus, and stereoacuity were not significant predictors of accommodative performance.

CONCLUSIONS. Overall, poor monocular accommodative performance of the amblyopic eye was associated with worse amblyopia and improved simultaneously with VA improvement, although there was variability across the study cohort. Further research is needed to determine the causal relationship between amblyopic eye VA and accommodation and its impact on amblyopia treatment.

Keywords: accommodation, amblyopia, amblyopia treatment

Amblyopia is the most common cause of monocular visual impairment in children and young and middle-aged adults.[1,2] In addition to decreased best-corrected visual acuity (VA) in the amblyopic eye, impaired accommodative performance has been widely noted in the literature, including reduced near point of accommodation,[3–5] decreased slope of the stimulus-response function,[6–10] and large steady-state error.[7,8] In a previous cross-sectional study,[11] we evaluated the accommodative accuracy of children with unilateral amblyopia aged 3 to 9 years using modified Nott retinoscopy. On average, these children had clinically significant accommodative lags at near when viewing monocularly with their amblyopic eyes compared with their nonamblyopic eyes and the eyes of children without amblyopia. This finding was consistent with previous studies of adults with amblyopia[6,7] and with one other cross-sectional study of children with amblyopia by Ukai et al.,[8] although children in that study did not wear optical correction, and the interocular differences in accommodative performance could, therefore, be related to unequal accommodative demands.

Better retinal image quality in the amblyopic eye during binocular viewing with optimal refractive correction has been shown to influence progression of improvement in amblyopic eye VA, even in the presence of strabismus.[12–14] An increased accommodative error for amblyopic eyes during monocular viewing is therefore of concern because it could result in degraded retinal image quality during patching therapy and potentially limit the effectiveness of amblyopia treatment. Previous case studies of adults[15–17] and older children[18] with amblyopia have demonstrated an association between amblyopic eye accommodative performance and VA after accommodative training, but there are minimal data regarding this relationship for young children with unilateral amblyopia or in the absence of accommodative training. Singh and Agrawal[19] assessed accommodation by determining whether near acuity improved in the presence of +3D lenses for a mixed group of 3- to 15-year-old children with unilateral and bilateral amblyopia. They concluded that patients with good accommodation (no change in acuity with addition of the lenses) showed a greater percentage improvement in amblyopic eye VA after patching. The objective of the present observational study was to evaluate changes in accommodative performance of children with unilateral amblyopia undergoing treatment.
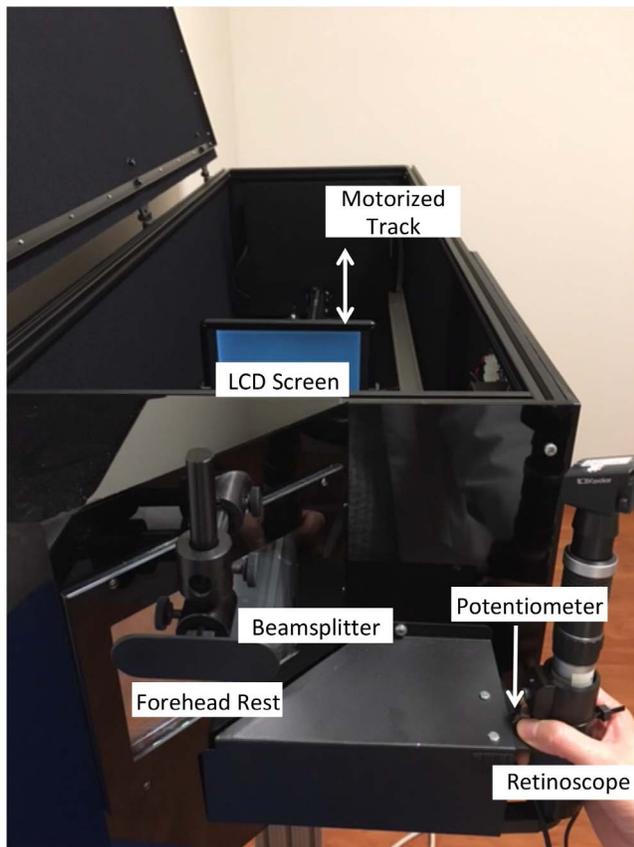
FIGURE 1. The modified Nott retinoscopy system (with the top lid open). The participants placed their head against the forehead rest while viewing the LCD screen at different distances on the track through the beamsplitter. The retinoscopist found the distance at which the reflex was neutral using reflection from the beamsplitter and then recorded the distance using a potentiometer by pressing a button. The limits of the linear potentiometer were 0.68 D at the far distance and 3.69 D at the close distance. Refractive states outside this range could not be measured and were assigned to the limit value.

METHODS

The study was conducted according to the tenets of the Declaration of Helsinki, at Southern California College of Optometry (SCCO) at Marshall B. Ketchum University and Indiana University School of Optometry (IU). The protocol and Health Insurance Portability and Accountability Act (HIPAA)-compliant informed consent forms were approved by the institutional review boards at each site, and the parent or legal guardian of each study participant gave written consent. Assent was obtained for those participants who were 8 years and older.

The study cohort consisted of children from 3 to 10 years of age at enrollment. All children had received comprehensive eye examinations including cycloplegic refraction at a routine clinic visit within 6 months prior to enrollment. Participants' habitual refractive correction had to meet the following criteria, compared with their cycloplegic refraction: (1) hyperopia not undercorrected by more than 1.5 diopters (D), (2) spherical equivalent (SE) within 0.5 D of full anisometropia, (3) cylinder power within 0.5 D of full astigmatism, and (4) cylinder axis within 6 degrees when cylinder power was ≥1.0 D. Participants who required refractive correction wore it for at least 4 weeks before enrolling into the study. None of the participants in either group had coexisting systemic conditions associated with reduced accommodation (e.g., Down syndrome, cerebral palsy) or were taking medications known to affect accommodation.

At diagnosis, participants in the amblyopic group had had an amblyopic eye VA of logMAR 0.3 (20/40) or worse with an interocular difference (IOD) of at least two lines, and the presence or documented history of strabismus and/or anisometropia (SE hyperopic anisometropia of ≥1.00 D; SE myopic anisometropia of ≥3.00 D; or astigmatic anisometropia of ≥1.50 D). During the study, all participants with amblyopia received amblyopia treatment (refractive correction with or without patching therapy) as prescribed in routine clinical care. None of the participants received atropine therapy. Participants in the group with typical vision were required to have age-normal visual acuities in both eyes (logMAR 0 [20/20] or better if >8 years, logMAR 0.2 [20/30] or better if ≥6 to ≤8 years, logMAR 0.3 [20/40] or better if 3 to <6 years of age),[20] an interocular difference in acuity of no more than one line, and no strabismus or amblyogenic anisometropia, as defined above.

Study Procedures

Each time the participants with amblyopia returned for a routine clinical follow-up visit, they also participated in a study follow-up visit. The following information was obtained from the clinical record: associated amblyogenic risk factor(s), cycloplegic refraction, habitual spectacle prescription, duration wearing latest refractive correction, and duration of patching treatment.

The study procedures were performed with participants wearing their habitual refractive correction, if any. The data were collected by the same examiner at each site (AMC at SCCO and VM at IU). Monocular distance VA was assessed using the Amblyopia Treatment Study visual acuity testing protocol with HOTV optotypes[21] on an electronic VA (EVA) test system. Stereoacuity was measured with the Randot Preschool Stereoacuity test at 40 cm (Stereo Optical, Inc., Chicago, IL, USA),[22] and ocular alignment was assessed with cover testing at 3 m and 40 cm (unilateral cover test to determine presence of strabismus and prism and alternate cover test to measure the magnitude of any deviation).

Accommodative responses were evaluated using modified Nott dynamic retinoscopy. The examiner determined the refractive state of the eye by adjusting her distance from the participant to neutralize the retinoscopic reflex. The participant viewed images with naturalistic spatial amplitude spectra[23] in a commercially available animated cartoon movie presented on a 15- × 8.5-cm LCD screen mounted on a motorized track (Fig. 1). A forehead rest was used to stabilize viewing distance. Consistent with the previous study,[11] the Nott dynamic retinoscopy technique was modified using a beamsplitter that allowed the examiner to be on the same optical axis as the cartoon images (Fig. 1). A linear potentiometer attached to the retinoscope enabled the distance between the examiner and the participant's eye to be recorded and stored automatically when the examiner pressed a button. The dioptric distance between the retinoscope and the participant's eye provided the refractive state of the eye, with a range of measurable values of between 0.68 and 3.69 D. The equipment used to provide these modifications was designed, manufactured, and calibrated at Indiana University School of Optometry.

The intraexaminer, intrainstrument, and intrasession repeatability of this approach was assessed in two small cohorts of amblyopic and control subjects in the previous study.[11] The interexaminer comparison performed on one prespresbyopic adult was also provided in the previous study. For the

intrasession repeatability analysis with the same examiner and the same instrument, a mean signed difference of −0.06 D (95% limits of agreement [LOA] = ±0.80 D) and a mean unsigned difference of 0.30 D were found for the participants with amblyopia. A mean signed difference of −0.08 D (95% LOA = ±0.48 D) and a mean unsigned difference of 0.19 D were found for the participants with typical vision. The repeatability for the participants with typical vision with this modified Nott retinoscopy approach was consistent with retinoscopy results reported previously for individuals with typical vision.[24,25]

Nott retinoscopy was performed along the horizontal and then vertical meridian, in binocular conditions followed by monocular conditions. In binocular conditions, the left eye was tested after the right eye at each viewing distance before moving to the next viewing distance. In monocular conditions, the right eye was tested at all distances before collecting any data from the left eye. The order of stimulus presentation for each participant was assigned pseudo-randomly to increasing accommodation (50 cm [2 D], 33 cm [3 D], and then 25 cm [4 D]) or decreasing accommodation (25 cm [4 D], 33 cm [3 D], and then 50 cm [2 D]) demands. The results (12 measurements for each eye) were pooled across direction. The examiner monitored the stability of accommodation continuously by noting any fluctuation of the retinoscopy reflex and would ask participants questions about the movie to encourage interest and steady fixation if necessary. Measurements were only taken when the reflex appeared stable.

Data Analysis

Each participant's residual uncorrected refractive error in the vertical and horizontal meridia was calculated by subtracting their habitual refractive correction from their cycloplegic refraction in those meridia. These values were then combined with the dioptric distance of the target to generate a total adjusted accommodative stimulus and with the retinoscopy results to generate a total adjusted accommodative response. The difference between the stimulus and response was calculated to determine the participant's accommodative error at each stimulus distance. A positive difference indicated a lag of accommodation and a negative difference indicated a lead of accommodation.

The accommodative performance of the participants with amblyopia was then summarized using two metrics: (1) the slope of the accommodative stimulus–response function and (2) the accommodative error for a total adjusted stimulus from 4 to <5 D (instances where uncorrected refractive error and stimulus distance combined to form a stimulus in that range). The accommodative stimulus–response function describes the change in accommodative response as a function of stimulus distance, and its slope was derived from an error-in-variables regression (Stata; StataCorp LLC, College Station, TX, USA) performed on the response across the three stimulus distances. When describing accommodative error, a total adjusted stimulus of 4 to <5 D was used because, in the previous cross-sectional study, amblyopes were observed to have the highest accommodative error for a 4-D stimulus, compared with 2-D and 3-D stimuli, under monocular viewing conditions.[11] In addition, using the error at 4 to <5 D-adjusted stimulus allowed us to gain insight into accommodative error for near tasks. For example, for a participant viewing the target at 50 cm (2 D), 33 cm (3 D), and 25 cm (4 D) with residual uncorrected hyperopia of 1.5 D, the total adjusted accommodation stimuli would be 3.5, 4.5, and 5.5 D, respectively. The response for the target at 33 cm would be included in the accommodative error analysis.

RESULTS

The amblyopic group consisted of 26 participants (mean age ± SD = 6.2 ± 1.4 years). At enrollment, amblyopic eye logMAR VA ranged from 0.1 (20/25) to 1.0 (20/200), with a median of 0.4 (20/50), whereas fellow eye VA ranged from −0.1 (20/16) to 0.2 (20/32), with a median of 0.0 (20/20). Eight participants' amblyopic eye VA had improved from the diagnosis visit to be better than 0.3 logMAR (20/40) before study enrollment. With regard to stereopsis at the enrollment visit, 12 (46%) children with amblyopia had no measurable stereopsis, 7 (26%) had 800″, 3 (12%) had 400″, and 4 (15%) had 100″. Of the 26 participants with amblyopia, 4 (15%) had strabismic amblyopia, 16 (62%) had anisometropic amblyopia, and 6 (23%) had combined-mechanism amblyopia. The SE refractive error of the amblyopic eye ranged from −1.00 to +7.63 D, with a median of +5.63 D, whereas the SE refractive error of the fellow eye ranged from +0.25 to +6.13 D, with a median of +2.25 D. The Table shows the clinical characteristics of each participant in the amblyopic group. The number of follow-up visits ranged from one to five (median of two), and the duration of follow-up ranged from 1 to 19 months (median, 5 months).

The group with typical vision consisted of 10 participants (mean age, 6.3 ± 2.4 years), who came for two study visits separated by between 1 and 17 months (7 participants had more than 1 year between visits). Their logMAR visual acuities ranged from −0.1 (20/16) to 0.1 (20/25) (median of 0 [20/20]) in both the better and worse eyes, which were assigned randomly for participants with equal acuity in the two eyes. All participants in the control group had stereoacuity of 100″ or better. None of these participants wore glasses. Their SE refractive error ranged from +0.25 to +1.5 D, with a median of +0.75 D in the better eye, and from +0.25 to +1.75 D, with a median of +0.75 D in the worse eye, with astigmatism of less than 1.0 D and SE anisometropia of less than 0.5 D for all participants.

A total of 1824 accommodative response measurements were attempted for the participants with amblyopia and 480 for the participants with typical vision. Ninety-one measurements from the participants with amblyopia and 11 measurements from the participants with typical vision could not be collected, primarily due to the limited range of the potentiometer. In the group with amblyopia, 52 of the 91 missing values were from the amblyopic eyes (37 due to accommodative responses that did not reach the more distant end of the measurement range [<0.68 D], 14 due to accommodative responses that were closer than the measurement range [>3.69 D], and 1 measurement was not collected), whereas 39 of the 91 missing points were from the fellow eyes (20 due to more distant accommodative responses than the measurement range and 19 due to accommodative responses closer than the measurement range). In the group with typical vision, seven accommodative responses were closer than the measurement range and four were not collected. For the purposes of the data analysis, the responses more distant than the measurement range were assigned the limit value of 0.68 D before adjustment for uncorrected refractive error, and those closer than the measurement range were assigned the limit value of 3.69 D before adjustment. These measurements are identified with X symbols in the figures.

The accommodation data collected from the horizontal and vertical meridia were not qualitatively different from each other and, therefore, only data from the vertical meridian are presented in the figures and analyses. Total adjusted accommodative responses as a function of total adjusted accommodative stimulus for all visits from all participants are presented in Figure 2. The data from the participants with amblyopia were divided into three subgroups based on the amblyopic eye

TABLE. Clinical Characteristics of Participants With Amblyopia

Participant No.	Age, y	Habitual Spectacles	Cycloplegic Refraction	Type of Amblyopia	Visual Acuity at Enrollment, logMAR	Stereoacuity at Enrollment, arcsec	Amblyopia Treatment*
1	5.6	OD +2.50 Sph OS +2.25 Sph	OD +3.50 Sph OS +3.25 Sph	Strabismic	OD 0.2 OS 0	800	2 hours of daily patching
2	5.1	OD +0.25 −0.50 × 180 OS +5.00 −0.50 × 180	OD +1.25 −0.75 × 180 OS +6.00 −0.50 × 180	Anisometropic	OD 0 OS 0.3	800	2 hours of daily patching
3	6.2	OD +2.75 Sph OS +2.75 Sph	OD +2.75 −0.25 × 180 OS +2.75 −0.25 × 180	Strabismic	OD 0 OS 0.2	200	2 hours of daily patching
4	9.2	OD +3.00 −1.00 × 075 OS +0.50 DS	OD +4.50 −0.50 × 075 OS +1.75 Sph	Anisometropic	OD 0.5 OS −0.1	Nil	2 hours of daily patching
5	8.4	OD Plano OS +1.75 Sph	OD +0.75 Sph OS +2.50 Sph	Anisometropic	OD −0.1 OS 0.4	100	2–6 hours of daily patching
6	4.6	OD +5.00 −1.75 × 180 OS +1.00 Sph	OD +6.50 −1.75 × 180 OS +2.50 Sph	Anisometropic	OD 0.4 OS −0.1	400	2 hours of daily patching
7	6.8	OD −0.75 −1.50 × 180 OS Plano	OD −0.25 −1.50 × 180 OS +0.50 Sph	Anisometropic	OD 0.3 OS −0.1	400	2 hours of daily patching
8	5.8	OD +0.75 Sph OS +4.00 Sph	OD +1.75 −0.25 × 180 OS +5.00 −0.25 × 180	Anisometropic	OD 0 OS 0.2	Nil	None
9	7.6	OD +4.00 Sph OS +0.25 Sph	OD +5.00 Sph OS +1.25 Sph	Anisometropic	OD 0.3 OS −0.1	100	None
10	4.3	OD +5.25 Sph OS +2.25 Sph	OD +7.00 −0.50 × 180 OS +4.25 −0.50 × 180	Mixed-mechanism	OD 0.2 OS −0.1	Nil	2 hours daily patching
11	5.3	OD +4.00 Sph OS Plano	OD +5.50 Sph OS +1.50 Sph	Anisometropic	OD 0.2 OS −0.1	400	2 hours daily patching
12	6.9	OD +5.50 −2.00 × 180 OS +7.50 −2.75 × 180	OD +7.00 −2.00 × 180 OS +9.00 −2.75 × 015	Mixed-mechanism	OD −0.1 OS 0.3	800	2 hours daily patching
13	8.7	OD +3.75 −1.00 × 150 OS +0.50 Sph	OD +4.75 −1.00 × 150 OS +1.50 Sph	Anisometropic	OD 0.2 OS −0.1	100	2 hours daily patching
14	7.3	OD Plano OS +4.00 Sph	OD +0.25 Sph OS +4.25 −0.50 × 180	Mixed-mechanism	OD −0.1 OS 1.0	Nil	6 hours daily patching
15	5.6	OD +6.75 −2.50 × 170 OS +7.25 −3.00 × 010	OD +7.25 −2.25 × 170 OS +7.75 −3.00 × 010	Strabismic	OD 0.2 OS 0.6	Nil	2 hours daily patching
16	4.7	OD +0.50 −0.50 × 180 OS +5.00 −1.50 × 180	OD +2.00 −0.50 × 180 OS +6.50 −1.50 × 180	Anisometropic	OD −0.1 OS 0.4	800	2 hours daily patching
17	4.7	OD +5.50 −0.50 × 180 OS +7.50 −1.50 × 180	OD +5.50 −.50 × 180 OS +7.50 −1.50 × 180	Mixed-mechanism	OD 0 OS 0.5	Nil	2 hours daily patching
18	3.4	OD +6.50 −0.50 × 180 OS +4.75 −0.50 × 180	OD +6.50 −0.50 × 180 OS +4.75 −0.50 × 180	Mixed-mechanism	OD 0.8 OS 0.2	Nil	2–6 hours daily patching
19	5.6	OD +4.00 −0.50 × 180 OS +4.00 −0.50 × 180	OD +4.00 −0.50 × 180 OS +4.00 −0.50 × 180	Strabismic	OD 0.1 OS 0.4	Nil	2 hours daily patching
20	4.9	OD Plano −0.50 × 180 OS +5.25 −1.00 × 180	OD +1.00 −0.50 × 180 OS +6.25 −1.00 × 180	Anisometropic	OD 0 OS 0.4	800	None
21	6.7	OD +3.00 Sph OS +6.50 −0.50 × 180	OD +4.00 Sph OS +7.50 −0.50 × 180	Ansiometropic	OD −0.1 OS 0.3	Nil	2 hours daily patching
22	7.8	OD +3.50 Sph OS +7.00 −2.00 × 180	OD +5.00 Sph OS +8.50 −2.00 × 180	Anisometropic	OD 0 OS 0.7	Nil	2 hours daily patching
23	6.0	OD +5.00 −0.50 × 180 OS +6.50 −1.00 × 165	OD +5.75 −1.00 × 180 OS +7.25 −2.00 × 165	Mixed-mechanism	OD 0.1 OS 0.4	Nil	2 hours daily patching
24	6.5	OD +1.25 Sph OS +3.25 Sph	OD +2.25 Sph OS +4.25 Sph	Anisometropic	OD 0 OS 0.1	200	None
25	7.5	OD +6.00 Sph OS Plano	OD +6.75 Sph OS +0.75 Sph	Anisometropic	OD 0.8 OS 0	Nil	6 hours daily patching
26	5.9	OD +5.75 −1.50 × 180 OS +3.00 −0.50 × 180	OD +7.25 −1.50 × 180 OS +4.50 −0.50 × 180	Anisometropic	OD 0.2 OS 0	400	None

* Amblyopia treatment prescribed by the participant's eye care provider other than refractive correction during the study period.

VA at the relevant visit: (1) amblyopic eye VA better than 0.3 logMAR (20/40), (2) amblyopic eye VA of 0.3 to 0.4 logMAR (20/40 to 20/50), and (3) amblyopic eye VA worse than 0.4 logMAR (20/50). The total adjusted accommodative response data collected in binocular viewing are presented in Figures 2A–2D and in monocular viewing in Figures 2E–2H. The data from the better and worse eyes of the group with typical vision and the fellow and amblyopic eyes of each amblyopic subgroup are presented for comparison. An error-in-variables linear regression (Stata; StataCorp LLC) was performed on each
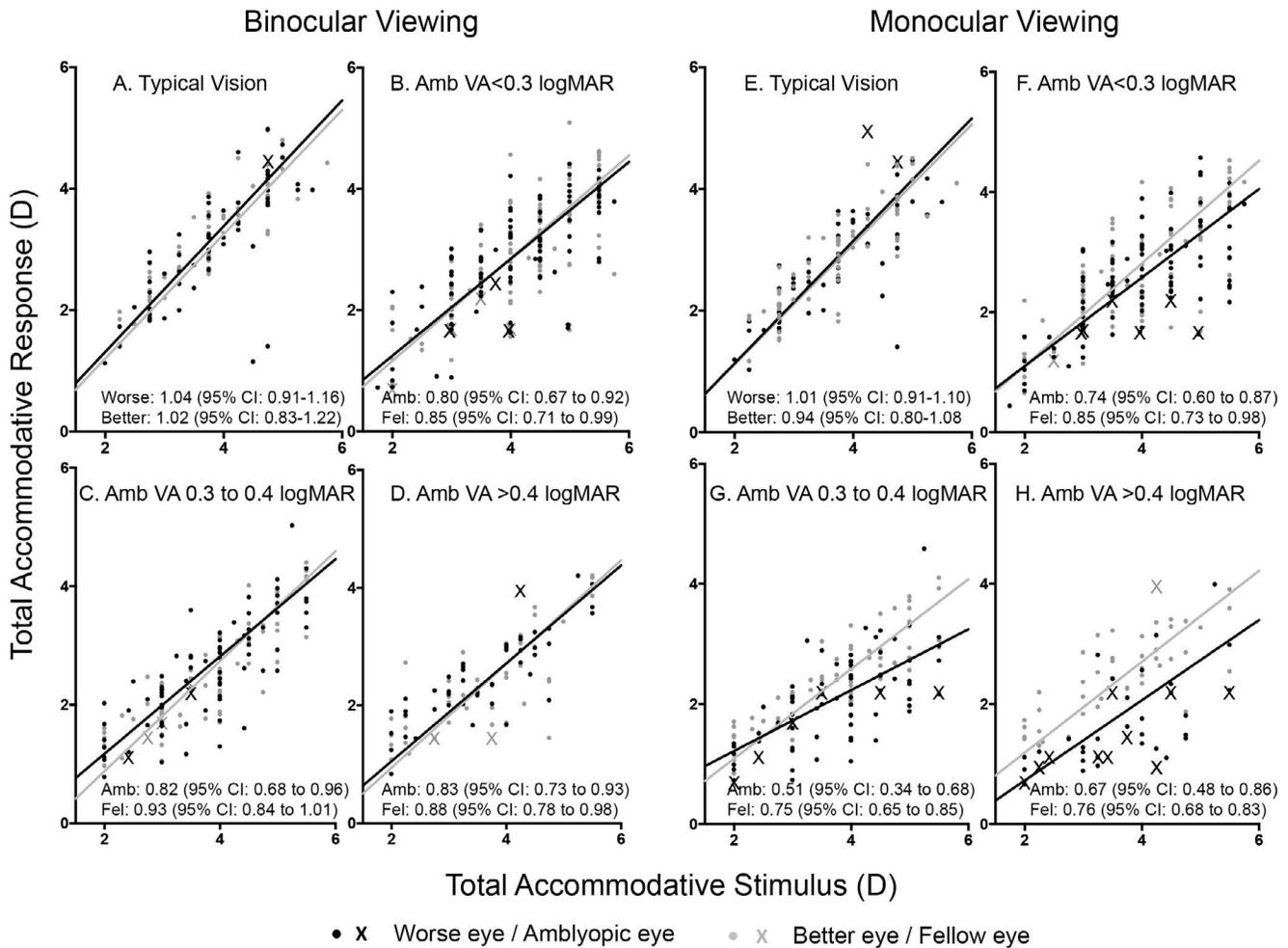
FIGURE 2. Total adjusted accommodative response (measured refractive state of the eye plus residual uncorrected refractive error) as a function of total adjusted accommodative demand (target demand plus residual uncorrected refractive error), as measured in the vertical meridian, for participants with typical vision and those with amblyopia, under binocular (**A–D**) and monocular viewing (**E–H**) from all visits. Data from the participants with amblyopia were grouped according to amblyopic eye visual acuity at the visit (<0.3 logMAR, 0.3 to 0.4 logMAR, and >0.4 logMAR). Each data point presents a single participant's eye for one visit (in other words, a participant whose amblyopic eye VA at two visits fell within the same VA could have six data points on the figure). The "out of range" responses >3.69 D were assigned to 3.69 D and the responses <0.68 D were assigned to 0.68 D before adjustment for uncorrected refractive error (both represented with X symbols). The slopes of the fitted error-in-variables regression lines are provided at the *bottom* of each graph.

set of data, to incorporate the measurement error in estimating the participants' total accommodative stimulus. These regression slopes are provided in each panel. The amblyopic and fellow eyes of participants with amblyopia exhibited reduced accommodative accuracy compared to the participants with typical vision when viewing monocularly, with amblyopic eye performance tending to decrease with worse amblyopic eye VA. The slopes of the fitted stimulus-response functions were higher in the fellow eye than the amblyopic eye in monocular viewing in all three VA subgroups with amblyopia, but lower than the better/worse eyes of the participants with typical vision. In binocular viewing the slopes were more similar in the two eyes of each group, with the slopes from the participants with amblyopia being lower than those of the participants with typical vision.

The monocular viewing data from the enrollment visit and the last follow-up visit of the group with amblyopia are summarized using the individual accommodative stimulus-response function slopes in Figure 3 and accommodative errors for a total adjusted stimulus of 4 to <5 D in Figure 4, to evaluate how accommodation changed with change in amblyopic eye VA in each individual participant. A stimulus–response function indicating a response matched to the change in stimulus would have a slope of 1, whereas no change in response with the stimulus would result in a slope of 0. In the case of accommodative error, an accurate response would have an error of 0 D. In both Figures 3 and 4, the data are plotted as a function of the VA of the amblyopic eye at each visit. The data for each participant are connected and coded by the duration of patching treatment at each visit, with the enrollment visits represented by small symbols and the last visits by large symbols. The slopes and errors for the amblyopic eyes were quite variable when amblyopic eye VA was good (<0.3 logMAR), but performance was consistently poor at the worse amblyopic eye VAs. These slope and error metrics both tended to improve as the amblyopic eye VA improved with treatment, whereas the performance of the fellow eyes, although variable, remained more consistent on average as function of amblyopic eye VA.

Changes in accommodative stimulus–response function slope and accommodative error for the 4 to <5 D-adjusted stimulus under monocular viewing for both amblyopic and

Monocular Accommodative Stimulus-Response Function Slope at First and Last Visits
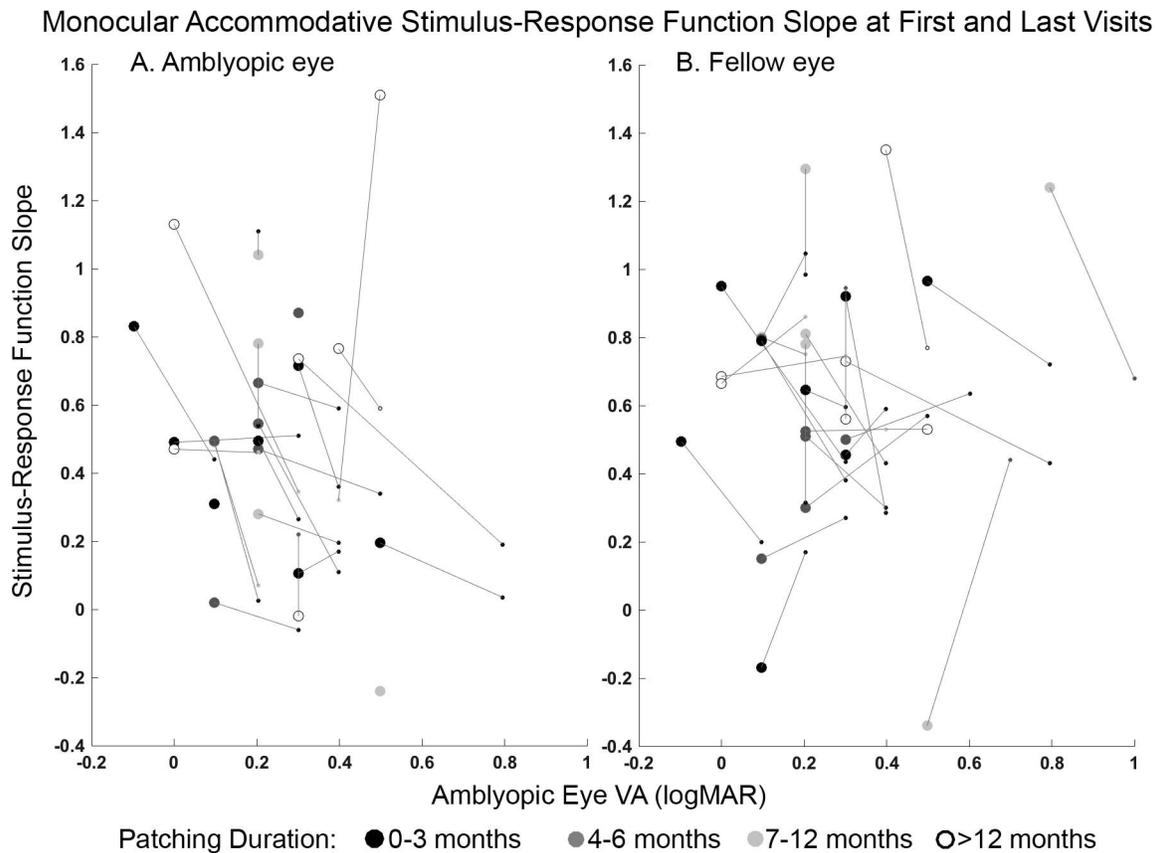

FIGURE 3. Monocular viewing accommodative stimulus–response function slopes at the first visit (*small symbols*) and last visit (*large symbols*) with coding for patching duration, for the amblyopic eye (**A**) and the fellow eye (**B**). In both cases, the slopes are plotted as a function of amblyopic eye VA at the relevant visit.

fellow eyes are plotted as a function of lines of improvement in the amblyopic eye VA between enrollment and the last follow-up visit in Figures 5 and 6, respectively. The data are coded by the VA of the amblyopic eye at the enrollment visit. A mean increase in slope of 0.24 [SD ± 0.34] in amblyopic eyes and a mean increase in slope of 0.09 [SD ± 0.35] in fellow eyes were observed with a mean improvement in amblyopic eye VA of 1.69 [SD ± 1.26] lines, implying a mean increase of 0.14 in slope in amblyopic eyes and 0.05 in fellow eyes per line of acuity improvement in the amblyopic eye. For accommodative error calculations, a mean reduction of 0.49 D [SD ± 0.87 D] in lag in amblyopic eyes and a mean reduction of 0.26 D [SD ± 0.48 D] in lag in fellow eyes were observed with a mean improvement in VA of 1.69 [SD ± 1.26] lines, implying a mean reduction of 0.29 D in lag in amblyopic eyes and 0.15 D in lag in fellow eyes per line of acuity improvement in amblyopic eyes. These values would only be likely to increase if the accommodative response measurements beyond the limits of the potentiometer were acquired.

Overall, the accommodative performance of the participants with amblyopia was summarized using four linear mixed models for the combination of amblyopic and fellow eyes under monocular and binocular viewing with total adjusted accommodative response as the dependent variable and individual participant as a random effect. The factors included in the models were stimulus demand, amblyopic eye VA at the visit when the data were recorded, age, time in the study, patching duration, stereopsis, and history of strabismus. The total adjusted demand and response data were both recentered around a value of 4 D to reveal the effects of the other variables relative to this "baseline" 25-cm near viewing distance.

Confirming the results shown in Figure 2, the amblyopic eyes on average showed 0.3 D less accommodation per diopter of change in accommodative stimulus under monocular viewing compared to binocular viewing (monocular coefficient of 0.25 versus binocular coefficient of 0.55, $P < 0.001$ in both cases). The effect of stimulus was more similar in monocular and binocular viewing for the fellow eyes (monocular coefficient of 0.70 versus binocular coefficient of 0.76, $P < 0.001$ in both cases). For amblyopic eyes in monocular viewing, the additional effect of amblyopic eye VA (0.14 D decrease in accommodative response per line of acuity loss, $P < 0.001$) was highly significant, as was the interaction between VA and accommodative stimulus (0.09 D of additional lag per diopter of stimulus, per line of acuity loss, $P < 0.001$), indicating that the increasing error with increasing demand was greater in the amblyopic eyes with poorer acuity (as shown in Fig. 2). The effect of amblyopic eye VA on responses of the amblyopic eye in binocular viewing was borderline significant (0.09 D less accurate for each line of VA reduction, $P = 0.01$), whereas the interaction between stimulus and VA was not significant for the accommodative response of the amblyopic eye in binocular viewing ($P = 0.23$). Neither patching duration ($P = 0.92$), length of time in the study ($P = 0.77$), nor their interaction ($P = 0.57$) was significant, indicating that the combination of viewing distance and VA were stronger predictors of accommodative performance of the amblyopic eye under monocular viewing regardless of how much treatment the participants received. The other variables included in the four models, participant's age (all $P > 0.11$), history of strabismus (strabismic/mixed or anisometropic amblyopia; all $P > 0.05$), and stereoacuity (all $P > 0.17$) were not significant predictors
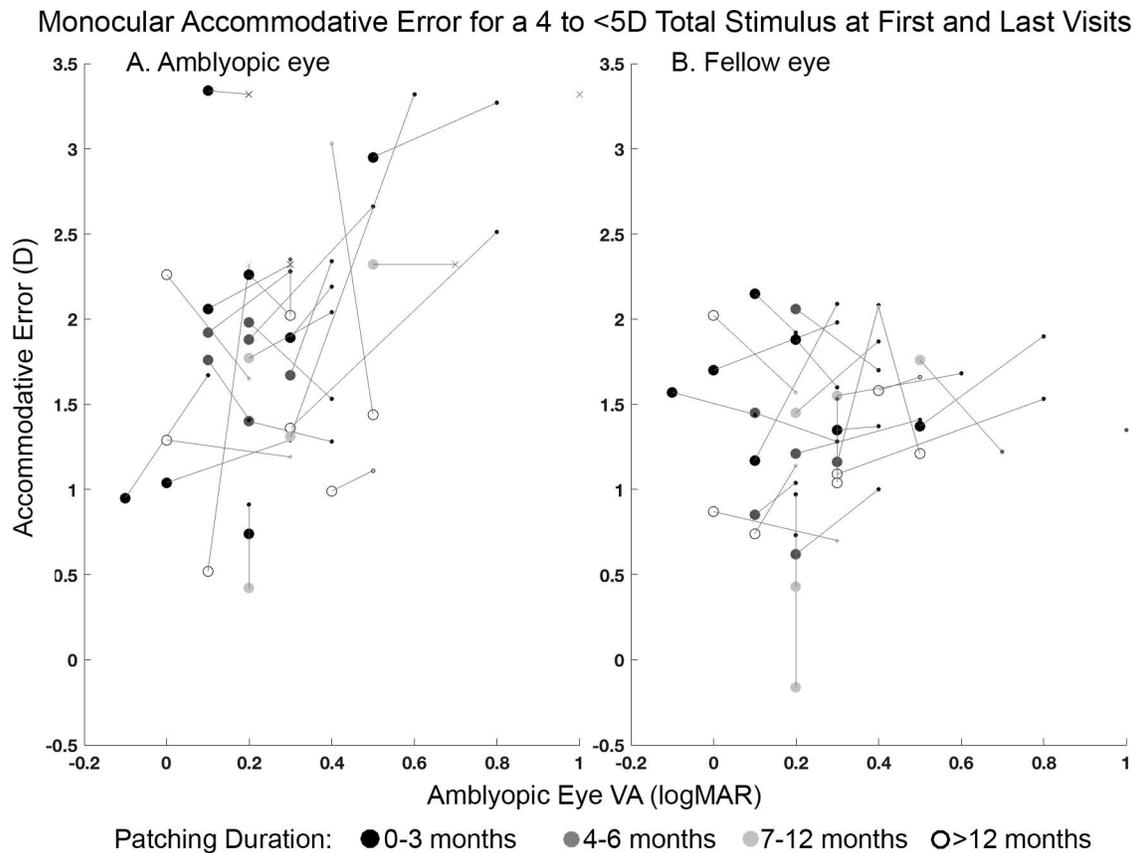
FIGURE 4. Monocular viewing accommodative error for a total adjusted stimulus of 4 to <5 D at the first visit (*small symbols*) and last visit (*large symbols*), with coding for patching duration, in the amblyopic eye (**A**) and the fellow eye (**B**). In both cases, the errors are plotted as a function of amblyopic eye VA at the relevant visit.

of accommodative performance for amblyopic or fellow eyes in monocular or binocular conditions.

DISCUSSION

In this study, we sought to understand whether the average monocular accommodative deficit in the amblyopic eye observed in our previous cross-sectional study would improve with VA improvement in individual participants. The study cohort included children of a wide range of ages and duration of glasses wear and/or patching treatment. Across these diverse characteristics, compared to children with typical vision, the children with amblyopia on average exhibited reduced accommodative performance for both fellow and amblyopic eyes in binocular viewing (Figs. 2A–2D), but their largest deficit was in their performance when viewing monocularly with their amblyopic eye (Figs. 2E–2H). This is consistent with our previous study.[11] The increased accommodative errors for the amblyopic eye at higher accommodative demands, are also consistent with previous studies evaluating the accommodative performance of amblyopic children and adults.[6–11]

The children with the more severe amblyopia tended to exhibit more reduced stimulus–response function slopes and accommodative accuracy when viewing monocularly with their amblyopic eye (Figs. 3A, 4A). This relationship between the amblyopic eye VA and accommodation was not found in our previous cross-sectional study.[11] The previous and current studies included participants with the same range of amblyopia severity, but the current study had a within-participant

longitudinal design. The likely reason for this difference between the studies is the variability in accommodative behavior of individual participants. In general, accommodation improved as the amblyopic eye VA improved with treatment; however, we also observed some participants whose amblyopic eye VA improved without improved accommodation and some who showed improved accommodation with minimal improvement in VA. It is interesting to note the similarity between Figure 3 in the current study and figure 7 of Ukai et al.[8] Both figures demonstrate shallow stimulus–response function slopes at acuities poorer than approximately 20/60, with significant variability in slope at better acuities. Further investigations are necessary to better understand the variability of accommodation in children.

The general relationship between accuracy of accommodation and amblyopic eye VA over the course of amblyopia treatment observed in the present study has been reported in several case studies that evaluated the effectiveness of accommodative therapy in improving visual function in children and adults with amblyopia. These case studies have demonstrated that steady-state accommodation improves with VA following accommodative therapy.[15,16,26,27] The main difference between the present study and the previous case series is that the participants in the current study did not receive any specific accommodative therapy. To our knowledge, this is the first study that evaluates the relationship between accommodation and amblyopic eye VA during conventional amblyopia treatment (refractive correction with or without patching) in children. In this study, as shown in Figure 2 and the mixed model analyses, amblyopic eyes exhibited significantly less accommodation under monocular
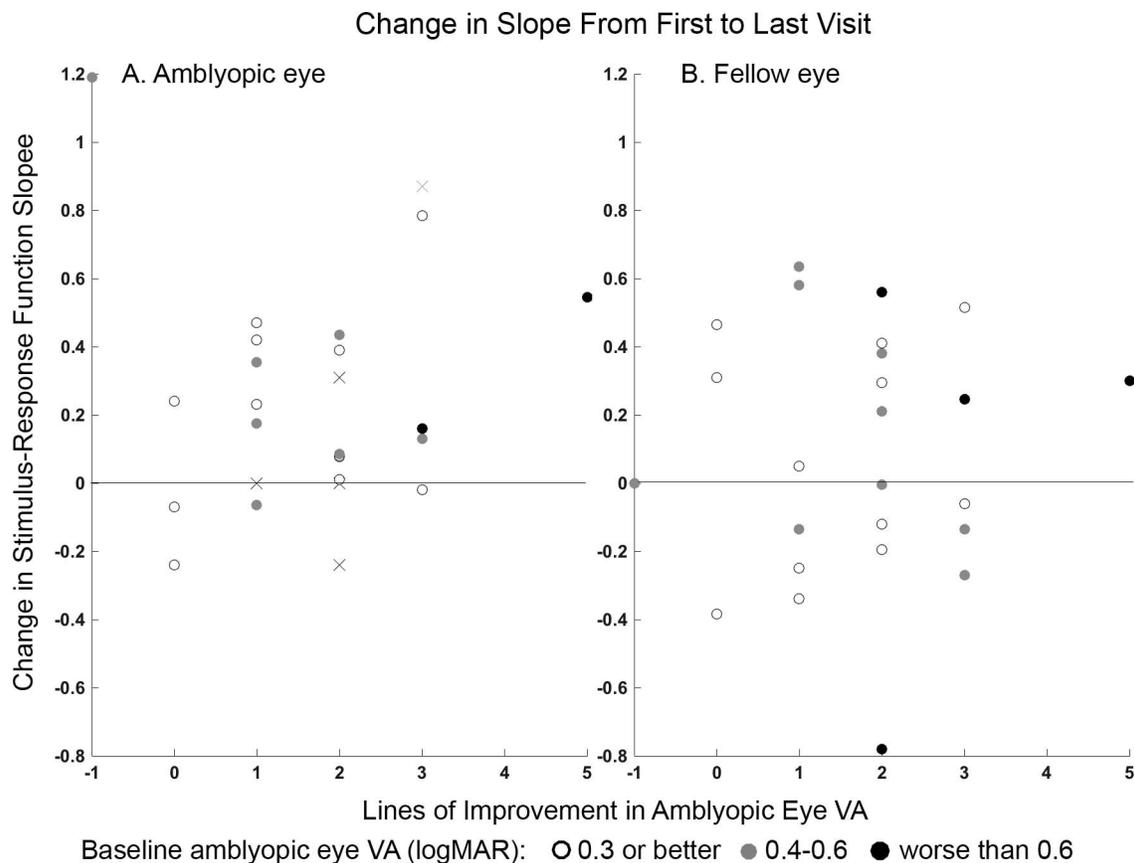
FIGURE 5. Change in monocular viewing stimulus response function slope from the first to last visit as a function of lines of improvement in the amblyopic eye VA. Data falling above the line indicate increase in slope from the first to the last visit. (**A**) Measurements from the amblyopic eyes. (**B**) Measurements from the fellow eyes.

viewing (versus binocular viewing) and with worse amblyopic eye VA. For the relatively small sample size and the diverse characteristics of the participants in the current study, time in the study, patching duration, age of the participant, stereopsis, and history of strabismus were not significant predictors.

Two primary hypotheses, motor and sensory, have been proposed to explain the etiology of poor monocular accommodative performance in an amblyopic eye.[8,28,29] The purely motor hypothesis would predict a deficient efferent pathway and output of the accommodative system. However, we observed more accurate responses from the amblyopic eye in binocular viewing conditions than monocular conditions, indicating that the amblyopic eye is capable of improved accuracy. This study therefore, along with previous studies,[4,7,11,30] supports the sensory hypothesis, in which accommodative performance improves with better sensory input (i.e., improved VA), rather than a purely motor explanation for the etiology of poor monocular accommodative performance in the amblyopic eye.

Based on the sensory hypothesis, we would predict that accommodative performance in monocular conditions would improve when amblyopic eye VA improves with amblyopia treatment. However, this relationship was not observed consistently in all participants. Some participants showed improved accommodative accuracy when their amblyopic eye VA improved with treatment and some showed the reverse (Fig. 4). Beyond any impact of measurement error or eccentric and unsteady fixation,[5] there are a number of potential mechanistic theories about this relationship. For example, in the extreme, poor accommodative performance related to

poor amblyopic eye VA could result in a poorly focused retinal image during patching treatment, which could then limit the improvement in VA, and so both accommodative performance and VA would stabilize with a deficit in performance. Alternatively, acuity and accommodative performance could improve together in concert, each permitting the other to improve iteratively, or typical fluctuations in accommodative accuracy could provide sufficiently focused retinal images for short periods of time to drive improvement in acuity and then more sensitive accommodation performance. Given this range of possibilities, the variability in the empirical data and the trend for accommodative performance to improve with improvement in acuity in the data, it is appropriate to ask whether accommodative performance is likely to have an impact on the success of patching therapy. It was not possible to address this question using the current observational dataset, as a result of the relatively small sample size and diversity in participant characteristics and treatment. Lastly, the age at which the participants were first given refractive correction was not known, and, therefore, the impact of duration of optical correction on response to treatment and accommodation is unknown.

It is also interesting to note the variability in accommodative performance of the fellow eyes of the amblyopes in Figures 3 and 4. These eyes had typical acuities and therefore should not have had reduced performance as a result of poor sensory information. These observations for the fellow eye are not predicted by the sensory hypothesis (e.g., Kirschen et al.[6]). The optimal focus of the eye will depend on factors such as pupil size and ocular aberrations, both of which change with

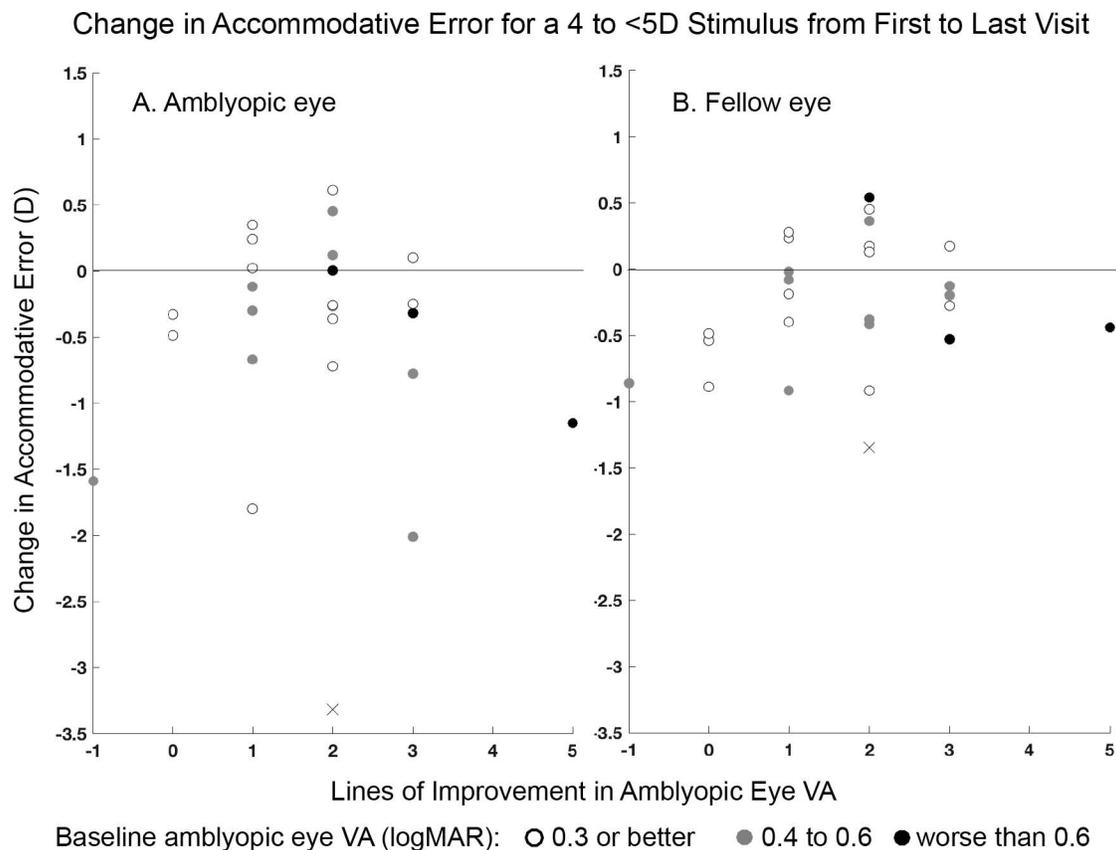## Change in Accommodative Error for a 4 to <5D Stimulus from First to Last Visit

FIGURE 6. Changes in monocular viewing accommodative error for a total adjusted stimulus demand of 4 to <5 D from the first to last visit as a function of lines of improvement in the amblyopic eye VA. Data falling below the line indicate reduced lag at the last visit. (A) Measurements from the amblyopic eyes. (B) Measurements from the fellow eye.

changing accommodation. The underlying factors driving the fellow eye performance remain to be determined.

In the present study, all of the participants had a VA of 1.0 logMAR (20/200) or better in their amblyopic eye, and a spatially broadband cartoon was used as the target to ensure that eyes with varying levels of amblyopia were provided with visible naturalistic spatial content. Another alternative would have been to provide a target only consisting of fine spatial detail to drive a maximal accommodative response. The goal here, however, was to gain understanding of the participants' likely behavior while looking at typical visual images. The fact that the accommodative performance of the amblyopic eye improved in binocular viewing conditions (presumably due to accommodation driven by the fellow eye) might at least in part explain the recent observations of improvement in acuity when performing binocular forms of amblyopia therapy in which the fellow eye has the potential to drive improved accommodation in the amblyopic eye,[31,32] and observations of improvement in acuity with refractive correction treatment alone[12,13] where the fellow eye can also drive accommodation in the amblyopic eye.

This preliminary observational study was an extension of our previous cross-sectional study and sought to evaluate the relationship between accommodation and amblyopic eye VA for patients with unilateral amblyopia. Although participant characteristics and treatment strategies were diverse, accommodation improved somewhat with amblyopic eye VA. In particular, patients with VA worse than approximately 0.5 logMAR (20/60) were more likely to have poor accommodation and be at risk for poor retinal image quality during monocular viewing. Interestingly, patients with better acuity showed more

variable accommodation and tended to display a range of monocular accommodative performance. To our knowledge, this is the first study that evaluates changes in accommodation during conventional amblyopia treatment (refractive correction with or without patching) in children. Future masked clinical studies could evaluate the role of accommodative performance in residual amblyopia, determine the efficacy of accommodative therapy or use of bifocals on success of patching therapy, and further identify the characteristics of patients who are most impacted by accommodative performance.

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