Delayed Correction for Extrapolation in Amblyopia

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Purpose. It has been suggested that amblyopes present impaired motion extrapolation mechanisms. In this study, we used the flash grab effect (FGE), the illusory mislocalization of a briefly flashed stimulus in the direction of a reversing moving background, to investigate whether the amblyopic visual system can correct overextrapolation.

Methods. Thirteen amblyopes and 13 control subjects participated in the experiment. We measured the monocular FGE magnitude for each subject. Two spatial frequency (2 and 8 cycles), two texture configurations (square wave or sine wave), and two speed conditions (270 degrees/s and 67.5 degrees/s) were tested. In addition, control subjects were further tested in reduced luminance conditions.

Results. Compared with controls, amblyopes exhibited a larger FGE magnitude both in their fellow eye (FE) and amblyopic eye (AE). The FGE magnitude of their AE was significantly larger than that of the FE. In a control experiment, we observed that the FGE magnitude increases with the decreasing of the luminance. The FGE magnitude of amblyopes fall into the same range as that of controls under reduced luminance conditions.

Conclusions. We observed a lager FGE in patients with amblyopia, which indicates that the amblyopic visual system does not accurately correct the overextrapolation when a moving object abruptly reverses its direction. This spatiotemporal processing deficit could be ascribed to delayed visual processing in the amblyopic visual system.

Keywords: amblyopia, flash grab effect, motion extrapolation

Amblyopia is a neurodevelopmental defect that arises from anomalous visual experience during the sensitive period of brain development in early life. Extensive evidence has demonstrated that amblyopes not only have typically poor spatial vision (e.g. visual acuity,[1] contrast sensitivity,[2] and binocular combination),[3] but that they also experience visual deficits in the temporal domain. For example: decreased temporal resolution[4] and increased temporal synchrony thresholds[5] have been identified in the amblyopic eye (AE). However, the fellow eye (FE) of patients with unilateral amblyopia may also exhibit synchrony processing[6] and motion discrimination[7] deficits. Those could be associated to an interocular delay in amblyopia, which can be characterized by a spontaneous motion-in-depth Pulfrich phenomenon.[8-10] With magnetoencephalography, Chadnova et al. reported an interocular processing delay of approximately 20 ms in patients with amblyopia.[11] These evidences suggest that the temporal processing deficits in amblyopia could be linked to a delay in visual information processing in the amblyopic brain.

Indeed, the neural processing of sensory input in the brain takes time. It is a challenge for the visual system to accurately localize moving objects due to the transmission delays between neurons and brain areas.[12] To overcome this, our brain may compensate for these intrinsic neural delays through motion extrapolation: predicting the present posi-

tion of a moving object by its past trajectory.[13,14] In a recent study, we investigated whether the amblyopic brain could compensate for internal neural delays by using a motion-induced illusion: the flash-lag effect.[15] We found that patients with amblyopia present a reduced flash-lag effect both in their AE and FE, which suggests that the amblyopic visual system presents a reduction in motion extrapolation.

However, what if an object's motion suddenly changes its direction, and the extrapolation becomes wrong? A motion reversal could make the previous extrapolation of the object's trajectory misleading. Nevertheless, we are usually unaware of perceiving the object's motion extrapolated beyond the end of its trajectory. This is because, in addition to the motion extrapolation mechanism, there is a "correction-for-extrapolation" mechanism in our visual system.[16-18] When the motion abruptly reverses, which violates the predicted trajectory, this mechanism would correct the extrapolation by shifting the perceived object location backward to its actual position. For instance, this correction-for-extrapolation mechanism could explain why, when an object moves back and forth, its trajectory appears shorter than it actually is.[18,19] In amblyopia, whether the amblyopic visual system, which presents reduced extrapolation, can correct the overextrapolation when the motion abruptly reverses its direction remains unknown.

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Here, by using another motion-induced illusion, the flash grab effect (FGE), we investigate whether such a correction-for-extrapolation mechanism is present in the amblyopic visual system. In a standard implementation of the FGE, an object is briefly flashed on a background annulus rotating back and forth at the timepoint when the motion reverses direction. Then, the flash would be perceived as shifted in the new direction of the moving background.[20] The motion-induced shift is independent of the presence of the flash, which only serves as a marker to measure this effect. In the present study, we assess the FGE monocularly in adults with unilateral strabismic and anisometropic amblyopia.

Previous behavioral and neurophysiological studies have suggested that several stimulus parameters, such as spatial frequency, blur, and speed, could modulate the time of visual processing and motion perception. High spatial frequency and sharp images may delay the speed of visual processing.[21–24] Stimuli with high speed may improve motion detection.[25] We additionally explore whether these visual parameters could affect the FGE perception in the delayed visual system of patients with amblyopia. Finally, as it has been reported that a reduced luminance increases the latency of the neural response in the visual system,[26,27] we further investigate whether a delay induced by a reduction in luminance can extend the FGE perception.

METHODS

Participants

Thirteen amblyopes (average age = 24 years old, range = 18–34 years old) and 13 control subjects (average age = 25 years old, range = 21–30 years old) with normal or corrected to normal visual acuity participated in this experiment. All participants, except the first author, were naïve to the experiment. The eye dominance of controls was defined by the Porta test. Amblyopia was defined as an interocular difference in the best-corrected visual acuity of strictly more than 0.1 logMAR (one line), and with a logMAR acuity of at least 0.0 in the FE. Anisometropia was defined as an interocular spherical equivalent difference of > 1 diopter, or cylinder difference of > 1.5 diopters. Strabismic amblyopia refers to the presence of an eye deviation of > 8 prism diopters. Mixed amblyopia refers to the presence of both anisometropia and strabismus. The clinical details of amblyopes are reported in the Table. This research complied with the tenets of the Declaration of Helsinki and had ethics approval from the Ethics Committee of West China Hospital of Sichuan University. Written informed consent was obtained from all participants before data collection.

Apparatus

The experiments were programmed and controlled on a MacBook Pro using Matlab R2018b (the Mathworks) with the PsychToolBox version 3.0.9 extension.[28,29] The stimuli were displayed on a gamma-corrected CRT monitor (SONY SUN GDM-5510, 21 inch) with a resolution of 1280 × 1024 pixels, refresh rate of 100 HZ, and mean luminance of 36 cd/m^2. The participants viewed the stimuli in a dimly lit room while wearing a dark opaque patch over the untested eye. The viewing distance was 57 cm.

Stimuli and Procedures

All the stimuli were presented on a gray background. An orange fixation point was presented at the center of the screen throughout the experiment. The flash grab stimulus consisted of an annulus with alternating black and white segments. The annulus had inner and outer radius of 2 and 3 degrees of visual angle (dva), respectively. The luminance contrast of the annulus was 0.5. The annulus rotated either clockwise or counterclockwise at an angular velocity of 67.5 degrees/s or 270 degrees/s and reversed direction every 670 ms with a 50 ms pause in motion at the reversal. At each reversal, a pair of orange or green colored discs (radius = 0.5 dva) were flashed in a random order for 10 ms (1 frame) superimposed on the annulus symmetrically from the vertical axis (Fig. 1A). Physical offsets, which were defined as the separation between the 2 pairs, were varied within 10 separation values (0, 10, 15, 20, 25, 30, 35, 40, 50, and 60 degrees) across trials. Each separation was tested with 20 repetitions, yielding a total of 200 trials/block. At the end of each trial, the stimulus disappeared, and the subject was asked to indicate whether they saw the orange pair clockwise or anticlockwise relative to the green pair by using a keyboard (see Fig. 1B).

Several physical parameters of the stimuli were tested: (1) two spatial frequencies: 2 and 8 cycles; (2) two texture configurations: square wave or sine wave modulations; (3) two speeds: 270 degrees/s (high) and 67.5 degrees/s (low). The low-speed conditions were only tested at the spatial frequency of eight cycles. Subjects were tested with the left eye and the right eye separately. In sum, there were a total of 12 conditions. We randomized the order of conditions for all subjects.

To investigate the influence of a delay induced by reduced luminance on the FGE, we additionally tested the control subjects with neutral density (ND) filters of different intensities: 1 ND (transmission rate = 10%) for all test conditions, and 2 ND (transmission rate = 1%) only for the condition with sinusoidal modulation with 8 cycles (*sine 8*) at both high and low speed. The ND filter was taped onto the glasses frame in front of the tested eye of the subjects during the tests. The order of the conditions was randomized.

Data Analysis

The data were analyzed with Matlab R2018b (the Math-Works). Psychometric functions of each participant's correct responses (seeing the orange pair of disks clockwise or anticlockwise relative to the green pair) as a function of the separation between the two pairs of disks were analyzed. Examples are illustrated for one control and one amblyopic subject in Figures 1C and 1D, respectively. Each psychometric function was fitted individually with a logistic function forced between 0 and 1. The main outcome was the point of subjective equality (PSE): the estimated midpoint of the logistic function at which participants perceived an alignment between the two pairs (see Fig. 1D). A significant PSE shift from zero would then characterize the FGE magnitude. The FGE could be expressed in space units (degrees), or converted into time units (milliseconds) as a function of the rotation speed of the stimulus (FGE magnitude in degree divided by stimulus speed).

All statistical analyses were performed using IBM SPSS Statistics, version 26.0 (Armonk, NY, USA). FGE magnitude was compared between groups using repeated measures

TABLE. Clinical Details of Amblyopic Subjects.

Subject	Age/Sex	Type	Eye	Refraction	VA (LogMAR)	Squint (PD)	Stereoacuity arc Seconds	History
A1	25/F	Aniso	FE (OD)	−1.75/−0.50 × 50 degrees	−0.1	∅	NA	Detected at 10 y old, patched for 2 y
			AE (OS)	+6.50/−2.50 × 10 degrees	0.7			
A2	31/M	Aniso	FE (OD)	+2.50	0	∅	200	Detected at 10 y old, no treatment
			AE (OS)	+4.25/−0.50 × 70 degrees	0.4			
A3	20/M	Mixed	FE (OD)	−5.50/−1.25 × 165 degrees	0	XT 25, R/L 5	NA	Detected at 4 y old, then received strabismic surgery at 7 y old, no patching
			AE (OS)	−1.25 × 10 degrees	0.3			
A4	22/M	Aniso	FE (OS)	−2.75	−0.1	∅	NA	Detected at 4 y old, patched for 1 y
			AE (OD)	+2.00	1.0			
A5	22/M	Aniso	FE (OS)	−2.50/−0.75 × 170 degrees	−0.1	∅	200	Detected at 8 y old, patched for 4 y
			AE (OD)	−1.75	0.1			
A6	18/M	Aniso	FE (OS)	−0.50 × 180 degrees	0	∅	NA	Detected at 5 y old, patched for 1 y
			AE (OD)	+3.50/+1.75 × 85 degrees	1.0			
A7	28/F	Aniso	FE (OS)	−0.50	0	∅	400	Detected at 15 y old, no treatment
			AE (OD)	+3.00/−0.50 × 90 degrees	0.7			
A8	34/M	Mixed	FE (OS)	−6.00/−0.50 × 175 degrees	0	ET 55, L/R 4	NA	Detected at 3 y old, then received strabismic surgery at 21 y old, no patching
			AE (OD)	−1.50/−1.50 × 180 degrees	0.8			
A9	19/M	Aniso	FE (OD)	+0.50 × 80 degrees	0	∅	400	Detected at 18 y old, no treatment
			AE (OS)	+3.50	0.2			
A10	22/F	Mixed	FE (OD)	−1.25	0	XT 17	NA	Detected at 12 y old, patched for 2 y, then received strabismic surgery at 21 y old
			AE (OS)	+6.50/−1.00 × 25 degrees	0.8			
A11	22/F	Strab	FE (OS)	−3.00/−0.50 × 110 degrees	0	ET 30	NA	Detected at 10 y old, patched for 2 mo
			AE (OD)	−5.00	1.0			
A12	24/M	Aniso	FE (OD)	−1.00/−1.00 × 15 degrees	0	∅	160	Detected at 15 y old, no treatment
			AE (OS)	+3.25/−2.75 × 170 degrees	0.4			
A13	25/F	Mixed	FE (OD)	−2.50/−0.50 × 150 degrees	0	XT 25	NA	Detected at 8 y old, then received strabismic surgery at 24 y old, patched for 1 mo
			AE (OS)	+1.50 × 100 degrees	1.0			

VA, visual acuity; FE, fellow eye; AE, amblyopic eye; Strab, strabismus; Aniso, anisometropia; EX, exotropia; ET, esotropia; PD, prism diopters; y, years; mo, months.
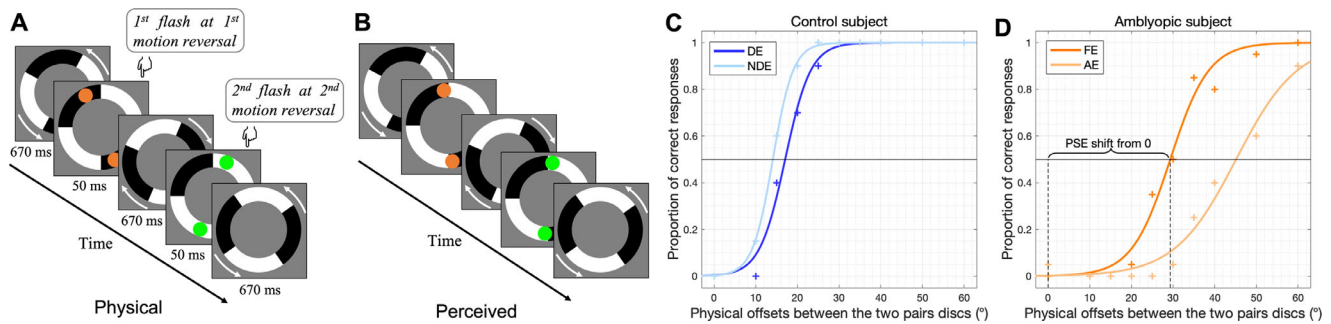
FIGURE 1. (**A**) An example of the physical stimuli of the flash grab effect (FGE) (spatial frequency is 2 cycles). An annulus rotated either clockwise or counterclockwise with reversal of direction every 670 ms. At each reversal point, a pair of colored discs (*orange* or *green*) were briefly flashed on the annulus in a random order. (**B**) The typical perception of FGE: the flashed discs' positions are shifted toward the new motion direction. (**C, D**) Psychometric function of the proportion of correct perception of the position of the *orange* pair relative to the *green* pair as a function of their separation for one representative participant from control and amblyopic groups, respectively. Data are fitted with a logistic function. PSE, point of subjective equality; FE, fellow eye; AE, amblyopic eye; DE, dominant eye; NDE, non-dominant eye.

ANOVA with group as the between-subject factor, and conditions as the within-subject factor. Within each group, the FGE magnitude was compared among the eyes, stimulus parameters, and luminance across all conditions using within subject repeated measures ANOVA. For post hoc analysis, two-sided Wilcoxon rank sum tests were used for comparison of the FGE difference between groups whereas two-sided Wilcoxon signed rank tests were used for within group comparisons. The level of significance was established at $P < 0.05$.

RESULTS

We first validated our FGE estimation by checking the quality of our fits and the significance of the PSE shift. The mean coefficient of determination R^2 was very high in all conditions: dominant eye (DE) 0.986 ± 0.01 (mean $\pm$ standard deviation) and nondominant eye (NDE) 0.988 ± 0.01 in the control group; FE 0.955 ± 0.05 and AE 0.864 ± 0.2 in the amblyopic group. The PSE shift from 0 was significant in all conditions for both control and amblyopic groups (for all $P < 0.001$) showing that a FGE was observable in all the conditions we tested.

In Figure 2, we illustrate the mean FGE magnitude with different stimulus conditions in the amblyopic and control groups. In general, the patients with amblyopia exhibited a larger FGE magnitude which was nearly twice that of controls (amblyopes = 36.5 ± 1.9 degrees, and controls = 19.9 ± 0.7 degrees, mean $\pm$ standard error). We performed between-subject repeated measures ANOVA tests with all conditions (6 levels) as a within-subject factor to compare FGE magnitude between the two groups. There were significant main effects for groups (AE versus NDE: $F_{1,24} = 14.25$, $P = 0.001$; and FE versus DE: $F_{1,24} = 5.641$, $P = 0.026$), and conditions (AE versus NDE: $F_{2.4, 57.8} = 21.87$, $P < 0.001$; and FE versus DE: $F_{2.1, 49.3} = 25.78$, $P < 0.001$) whereas the interactions of group and conditions were not significant (AE versus NDE: $F_{2.4, 57.8} = 2.11$, $P = 0.121$; and FE versus DE: $F_{2.1, 49.3} = 1.63$, $P = 0.206$). We subsequently conducted pairwise post hoc comparisons to further analyze these effects. In summary, (1) the FGE magnitude of AE in amblyopes was significantly larger than that of the NDE in controls in all test conditions ($P \leq 0.008$; see Fig. 2); (2) the FGE magnitude of FE in patients with amblyopia was significantly larger than

that of the DE in most conditions ($P \leq 0.048$; see Fig. 2) except under condition of *sine 2* ($P = 0.522$; see Fig. 2D).

To compare the FGE magnitude between the eyes of each group, we performed within subject repeated measures ANOVA tests with eyes (2 levels) and conditions (6 levels) as within-subject factors. The results show that the FGE magnitude was significantly different between the two eyes in the amblyopic group ($F_{1,12} = 8.63$, $P = 0.012$). The average FGE magnitude was 42.2 ± 2.9 degrees for the AE and 30.8 ± 2.2 degrees for the FE. In contrast, the difference of FGE magnitude between NDE and DE (20 ± 1 degrees vs. 19.8 ± 0.9 degrees) in the control group was not significant ($F_{1,12} = 0.16$, $P = 0.694$). A pairwise post hoc comparison found that the FGE magnitude differences between AE and FE in patients with amblyopia were significant in most conditions ($P \leq 0.033$; see Fig. 2) except in the condition *square 8* at low speed ($P = 0.116$; see Fig. 2C). In short, the FGE magnitude was larger for amblyopes compared to controls by 105.7 ms and, for patients with amblyopias, the FGE for the AE was larger than that of the FE by 66.6 ms.

The larger PSE in the amblyopic group reported here was accompanied by a shallower slope of the psychometric function in the AE (0.17 ± 0.02) compared to the FE (0.22 ± 0.02), which would be expected because of the reduced visual acuity of the AE. These should be independent from the PSE[30] and the differences in slope were actually much smaller than the differences observed in PSE. Furthermore, we did not observe any significant relationship between visual acuity and FGE (Supplementary Fig. S1) and we reported an extended FGE even in the FE of amblyopes despite their acuity being high (≤ 0.0 logMAR; see Fig. 2). Therefore, we are confident that the larger PSE observed in amblyopia is not the consequence of the reduced visual acuity of the AE. In order to check whether the presence of a strabismus could affect the FGE magnitude, we compared the FGE difference between the strabismic ($n = 5$) and non-strabismic patients with amblyopia ($n = 8$). However, we did not find any significant difference between strabismic and non-strabismic subgroups in all testing condition (for all $P \geq 0.38$).

To compare the FGE magnitude difference between the different conditions, we plotted the results for the different conditions of spatial frequency (Fig. 3A) and speed (see Figs. 3B, 3C) in the two groups. In the control group, the FGE
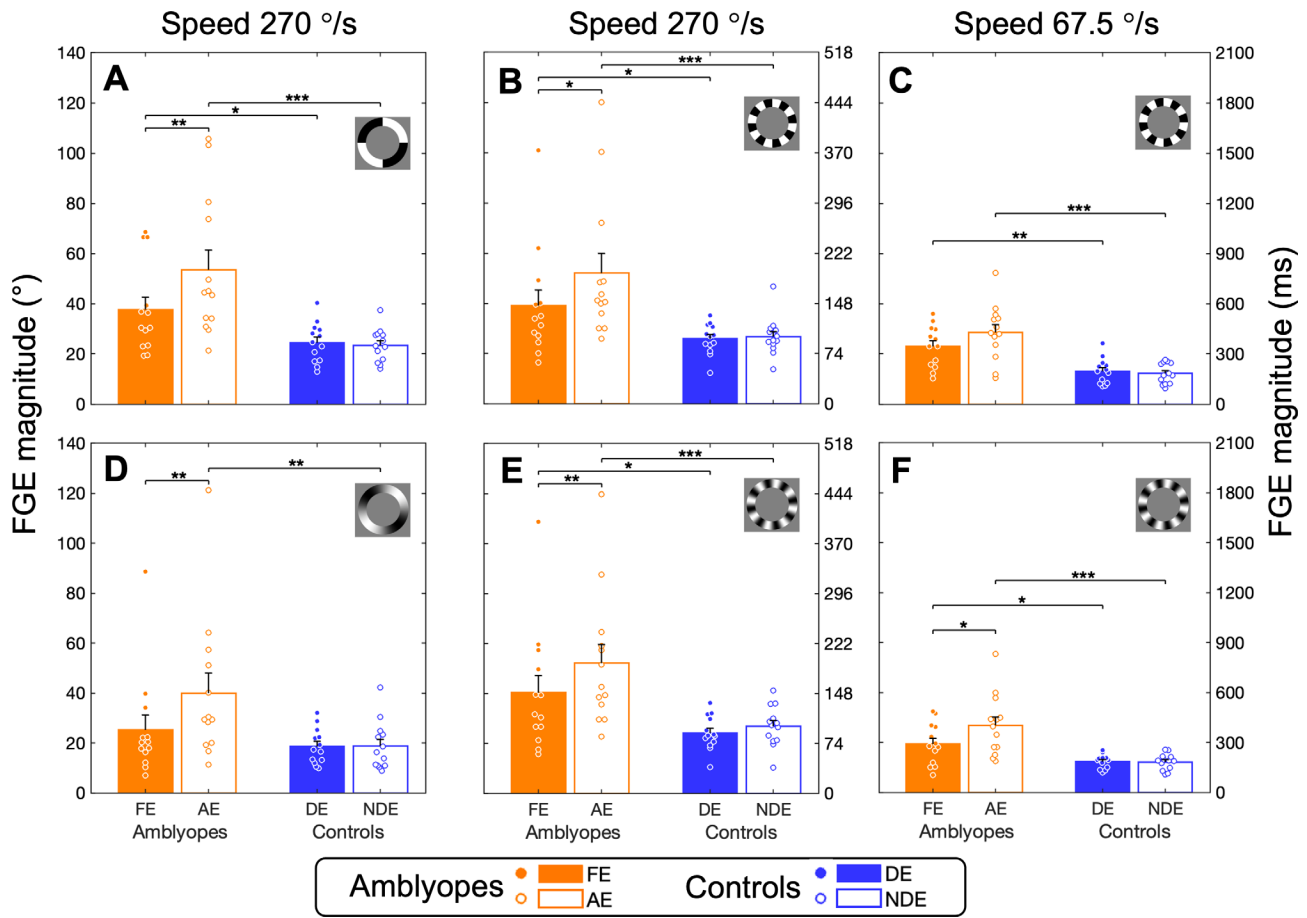
FIGURE 2. Mean FGE magnitude of the two groups under the different experimental conditions (**A–F**). The spatial frequency of each condition is illustrated at the *top right corner* in each panel. The *upper* and *lower* three panels represent the results of *square* and *sine* conditions, respectively. **A**, **B**, **D**, and **E** show the results of high-speed conditions (270 degrees/s), whereas **C** and **F** show the low-speed conditions (67.5 degrees/s). The *blue* and *orange* bars/circles represent the data of control and amblyopic groups, respectively. Individual data points for each subject are represented by circles. Results are compared between the eyes (*filled*: FE/DE and *open*: AE/NDE bars) of these two groups. FGE, flash grab effect; FE, fellow eye; AE, amblyopic eye; DE, dominant eye; NDE, non-dominant eye. Error bars represent standard error. ***$P \leq 0.001$; **$P \leq 0.01$; *$P < 0.05$. The left y-axis indicates the FGE magnitude in space units (degrees). The right y-axis indicates the FGE magnitude in time units (ms).
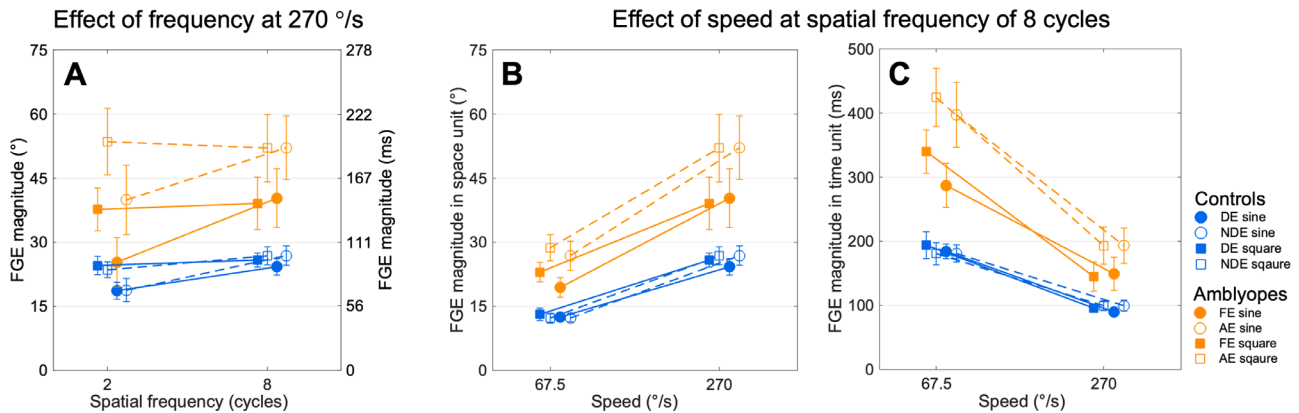

FIGURE 3. Mean FGE magnitude at different spatial frequency (**A**) and speed (**B, C**) conditions for the two groups. The FGE magnitude was reported in space units (degrees) or time units (ms). The *square* and *circle* dots represent square and sine wave texture of the rotating anulus, respectively. *Filled* and *open* dots represent the results of fellow eye (FE) and amblyopic eye (AE) for the amblyopic group (*orange*), and dominant eye (DE) and non-dominant eye (NDE) for the control group (*blue*). FGE, flash grab effect. Error bars represent standard error.
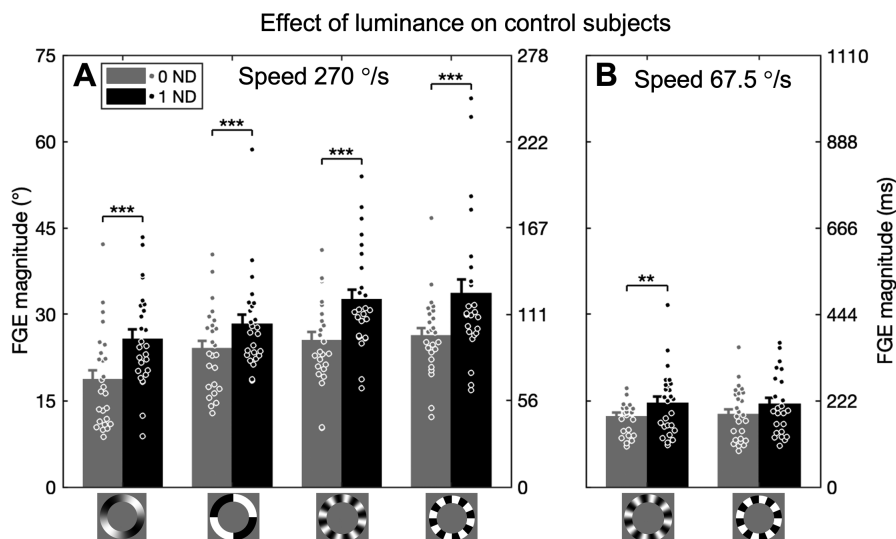
FIGURE 4. Mean FGE magnitude under different luminance conditions (0 ND and 1 ND) in the control group. Results are separately plotted for different speed conditions in panel (**A**) for 270 degrees/s; (**B**) for 67.5 degrees/s. Icons on the abscissa represent the stimulus texture in each condition. The different color blocks represent different luminance conditions (*gray* for 0 ND; *black* for 1 ND). Individual data points for each eye are represented by circles. FGE, flash grab effect; ND, neural density. Error bars represent standard error. ***$P \leq 0.001$; **$P \leq 0.01$. The left y-axis indicates the FGE magnitude in space units (degrees). The right y-axis indicates the FGE magnitude in time units (ms).

magnitude increases by approximately 20 ms with increasing spatial frequency for the sine wave texture (see Fig. 3A; $F_{1,12} = 23.12$, $P < 0.001$). Patients with amblyopia showed a similar tendency as spatial frequency increases ($F_{1,12} = 48.32$, $P < 0.001$), with even larger difference (approximately 50 ms; see Fig. 3A). However, there was no significant effect for square wave texture in both groups (controls: $F_{1,12} = 3.94$, $P = 0.07$; and amblyopes: $F_{1,12} = 0$, $P = 0.994$). In our task involving motion, space and time were separable. Therefore, we compared the group differences in FGE in space and time domains separately. When looking at the FGE expressed in spatial units, both groups exhibited an increasing FGE magnitude by approximately 20 degrees as the speed of the annulus increased (see Fig. 3B; controls: $F_{1,25} = 138.29$, $P < 0.001$; and amblyopes: $F_{1,25} = 36.39$, $P < 0.001$) which is consistent with the fact that a moving target with higher speed would cover a further distance. In contrast, when converted to time units, both groups showed a larger FGE magnitude by approximately 100 to 200 ms at low speed (see Fig. 3C). This would indicate that the FGE is actually shorter at high speed and that the FGE is inseparable in the space and time domains.

Next, we wanted to investigate whether the increase in FGE magnitude we observed could be mimicked by introducing a processing delay induced by a reduced luminance.[27] Luminance reduction was achieved using ND filters placed in front of the observers' eye. We analyzed the difference in FGE magnitude under the different ND conditions in the control group. Figure 4 shows the mean FGE magnitude tested with 0 ND and 1 ND across all experimental conditions. It appears that the FGE magnitudes with a 1 ND filter (24.9 ± 0.9 degrees) were significantly larger compared to 0 ND (19.9 ± 0.7 degrees, $F_{1,25} = 41.26$, $P < 0.001$). Pairwise post hoc comparisons showed that the differences were significant in all conditions (for all $P \leq 0.006$; see Fig. 4), except the condition of *square 8* at low speed ($P = 0.098$; see Fig. 4B).

To further investigate the influence of reducing the luminance on the FGE magnitude, we then tested 6 of 13 control subjects with a 2 ND filter under the sole conditions of *sine 8* at high and low speeds. The mean FGE at different luminance conditions (0 ND, 1 ND, and 2 ND) for this subset of participants is plotted in Figure 5. We found that the FGE magnitude increases with decreasing luminance for both speeds: 270 degrees/s (see Fig. 5A; $F_{1, 5.2} = 9.35$, $P = 0.026$) and 67.5 degrees/s (see Fig. 5B; $F_{2, 10} = 43.43$, $P < 0.001$). The mean increment in FGE magnitude for different neutral densities was 26.3 ms for 1 ND, and 145.6 ms for 2 ND. For comparison, we also reported the mean FGE magnitude of the amblyopic group (without the ND filter) under the same conditions as reference (see Fig. 5 orange dots). We can see that the FGE magnitude of the patients with amblyopia fall into the same range as that of the controls under the reduced luminance condition (see Fig. 5).

DISCUSSION

In this study, we used the FGE to investigate whether patients with amblyopia who are meant to show less extrapolation[15] could still correct for overextrapolation when the motion abruptly reverses its direction. We found that: (1) patients with amblyopia exhibit increased FGE magnitude both in their FE and AE compared to DE and NDE of controls, respectively. (2) For patients with amblyopia, the FGE magnitude of the AE is significantly larger than that of the FE. (3) In both the control and amblyopic groups, we observed that the FGE magnitude in space increases with increasing spatial frequency for the sine wave texture, and with increasing speed. (4) In the control group, the FGE magnitude increases with decreasing luminance.

In the human visual system, there is an intrinsic neural delay in visual information transmission through several processing stages.[12] Consequently, the brain needs time to process what we see. To accurately localize a moving object,
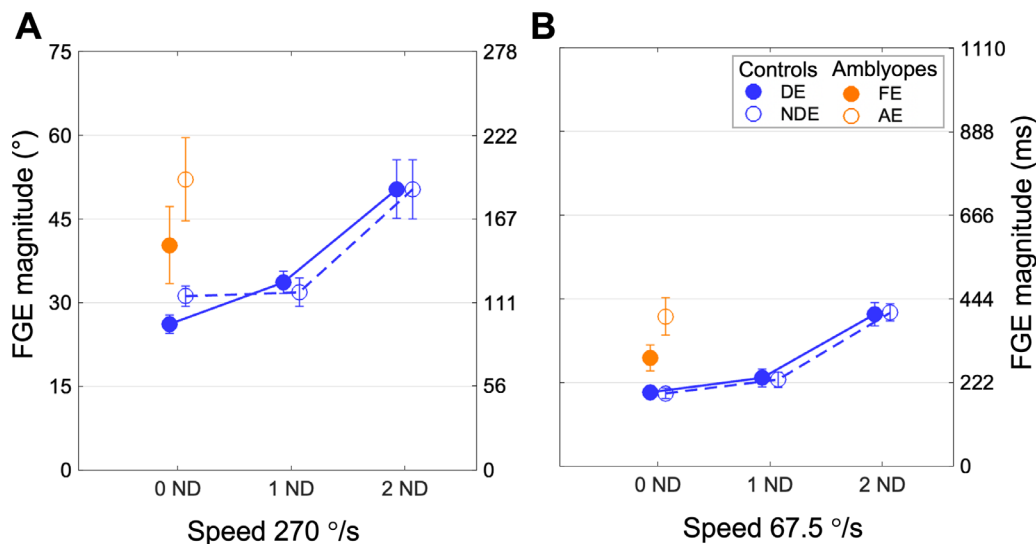
FIGURE 5. Mean FGE magnitude under different luminance conditions (0 ND, 1 ND, and 2 ND). Results are separately plotted with different speed conditions (**A** for 270 degrees/s; and **B** for 67.5 degrees/s). *Orange filled* and *open* dots represent the mean FGE magnitude of the FE and AE in the amblyopic group. *Blue filled* and *open* dots represent the mean FGE magnitude of the DE and NDE in the control group. FGE, flash grab effect; ND, neural density; FE, fellow eye; AE, amblyopic eye; DE, dominant eye; NDE, non-dominant eye. Error bars represent standard error. The left y-axis indicates the FGE magnitude in space units (degrees). The right y-axis indicates the FGE magnitude in time units (ms).

our brain must somehow compensate for the neural transmission delays. One way is through motion extrapolation: using the past trajectory of an object's motion to make predictions about its future location.[13] In a recent study, we found that patients with amblyopia present an impaired motion extrapolation mechanism in their visual system.[15] The ensuing question we ask here is whether the amblyopic brain can correct a wrong extrapolation incurred by an abrupt motion reversal?

The FGE illusion, a mislocalization of a flashed object in the direction of a reversing moving background, has been explained as a consequence of correcting for violated extrapolation.[18,31,32] The results of the current study show that patients with amblyopia do exhibit an FGE perception, which is that they perceive the flashed discs as displaced in the direction of the rotation of the annulus following the abrupt reversal. This finding answers the above question: the amblyopic visual system still can correct the extrapolation when the predictions are wrong. At the same time, however, the larger FGE magnitude in patients with amblyopia suggests that they may have inferior correction ability.

Based on previous neurophysiological animal studies about perceiving reversing stimuli,[33,34] Van Heusden et al.[35] proposed a model to explain the FGE illusion (Fig. 6). The brain uses the past motion information to predict the true position of a moving target (see Fig. 6A). When the motion abruptly reverses its direction, it takes time for the brain to detect the reversal. During that time, the motion trajectory continues to be extrapolated beyond the reversal point causing errors in prediction (see Fig. 6B). By the time the motion reversal is detected, there is a mismatch between the prediction and the actual position, which triggers the correction-for-extrapolation mechanism. As a result, the visual system corrects for the violated extrapolation and catches up by shifting from the predicted trajectory to the new one (see Fig. 6C). Based on this mechanism, any stationary object flashed at the reversal point would be erroneously corrected

and mislocalized, characterizing the FGE illusion.[20] Considering this, if there was a given delay in the visual system, the brain would take a longer time to process the visual input and detect the motion reversal. Consequently, the object would move even further along its actual trajectory before the visual system could catch up, thus, the position shift would be larger, leading to a larger FGE (see Fig. 6D).

Our results of testing different stimuli parameters support this delay hypothesis. We found a larger FGE at a higher spatial frequency and a smaller FGE with the square wave texture in both groups. These findings are in line with previous studies showing that high spatial frequency stimuli are processed slower,[21–23] and blurrier images are processed faster.[24] We also found that the FGE difference between low and high spatial frequency with sine wave stimuli was more marked in patients with amblyopia than controls. This may be due to the contrast sensitivity difference between low and high spatial frequency. Indeed, patients with amblyopia have very low sensitivity, and therefore probably have slower processing time at high spatial frequencies compared to both low spatial frequencies and controls.[2,36] Furthermore, the fact that patients' with amblyopia contrast sensitivity remains quite independent of spatial frequency for square-wave modulations, which encompass higher frequencies,[37,38] might explain the nonsignificant FGE difference between low and high spatial frequencies in the square wave conditions.

Additionally, the larger FGE observed in the space domain (see Fig. 3B) also fits the delay hypothesis. For a given delay, the target would have traveled further at high speed causing a larger prediction error and positional shift. The smaller FGE observed at high speed in the time domain (see Fig. 3C) could thus also illustrate faster motion discrimination and processing at high speed.[25,39]

To test the delay hypothesis, we investigated the effect of a delay induced by reduced luminance with ND filters on FGE perception. We observed that the FGE magnitude
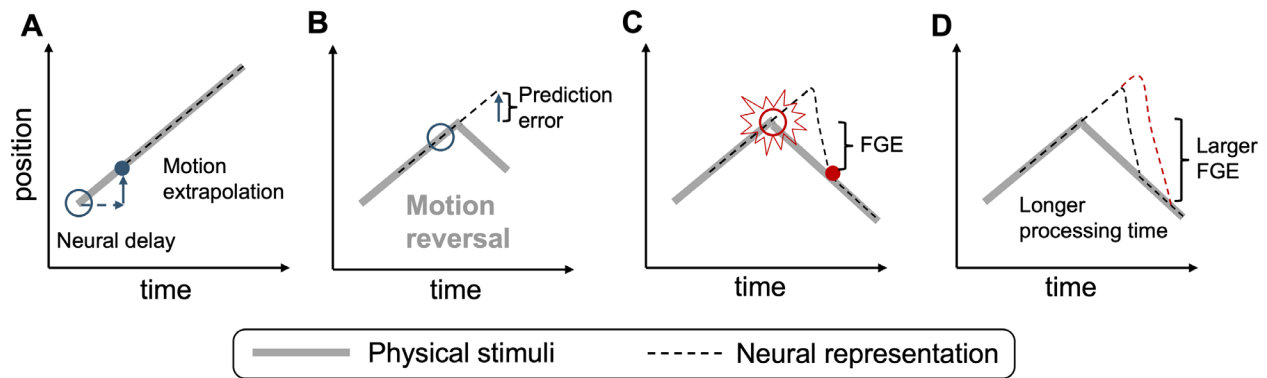
FIGURE 6. illustration of extrapolation in the flash grab effect (FGE) (adapted from Van Heusden et al.[35]). Each panel represents a target in space-time coordinates. Solid traces represent the trajectory of the physical stimulus, and the *dotted lines* indicate the mental representation of the same stimulus. (**A**) To accurately localize a moving object overcoming the neural delays, the visual systems would use the past motion trajectory to predict its true position (*blue circles and lines*). (**B**) When the motion abruptly reverses its direction, it takes time for the brain to detect the reversal, during which the motion could continue to be extrapolated beyond the reversal point, causing errors in predictions. (**C**) When the brain detects the reversal, the erroneous prediction and its actual position cause a mismatch, which triggers the visual system to correct the overextrapolation. If a stationary flash is presented at the same time as the reversal, it is erroneously corrected and mislocalized, resulting in the FGE. (**D**) If there is a given delay in the visual system, the brain takes a longer time to process visual inputs and detect the motion reversal. Consequently, the object moves even further along its actual trajectory before the change can be perceived, therefore the position shift would be larger leading to a larger FGE (*red line*).

did increase with a reduction in luminance (see Fig. 4, Fig. 5). A large body of evidence from electrophysiological, neuroimaging, and behavioral studies reported that reduced luminance prolongs response latency.[26,27,40–43] A delay introduced by a 1 ND filter varies between 10 and 20 ms.[27,42,43] Additionally, previous studies reported a delay of approximately 38 ms with filters of 1.5 ND,[40] and 83 ms for 1.8 ND.[44] In our study, we observed that the FGE magnitude was increased by 26.3 ms with 1 ND and by 145.6 ms with 2 ND. These values fall in the same range as the previously observed delays and strongly suggest that slowing down the processing of the visual system gives rise to a larger FGE percept.

Accumulating evidence shows that the amblyopic visual system is associated with temporal vision deficits, both in AE and FE processing. It has been reported that patients with amblyopia show poor performance in motion and temporal related tasks: temporal order perception,[45] synchrony processing,[6] and motion perception.[7,15,46] Black et al.[47] reported that children with amblyopia demonstrate slower visual processing with high-order visual tasks. Additionally, visual decision response times[48] and saccadic latency[49] are delayed in both the processing of the AE and the FE. These deficits in motion perception and processing delays could characterize a global processing delay in the whole amblyopic visual system. Such a global processing delay could explain the larger FGE we observed in the two eyes of amblyopes compared to controls.

In addition, we observed that the FGE magnitude of the AE was larger than that of the FE in the amblyopic group which may be due to a slower visual processing in the AE compared to the FE.[50–53] More specifically, an interocular delay between the FE and the AE has been reported psychophysically[8–10] and electrophysiologically using imaging techniques. Using functional magnetic resonance imaging (fMRI), Farivar et al. found that the cortical response to visual stimulation of the AE was delayed by approximately 500 ms relative to the FE.[54] In addition, a delay of 20 ms between the AE and the FE was found using magnetoencephalography.[11] The interocular difference in FGE between

AE and FE reported in our study (66.6 ms) falls in the same range as in those previous studies despite different visual tasks and experimental methods. Thus, we do believe that our finding of a larger FGE in the AE compared to the FE can also be explained by longer processing of the information specifically coming from the AE.

In our previous study, we observed deficits in extrapolation in both eyes of the amblyopic visual system which we attributed to abnormal alterations of the horizontal connections in V1.[15] In the current study, we found that patients with amblyopia exhibit deficits in correction for extrapolation. This could be explained both by a global processing delay in their visual system plus an additional specific delay in their AE. These results suggest that the extrapolation and correction for extrapolation are different processes that have different underlying mechanisms in the amblyopic brain.

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