

Children With Amblyopia Make More Saccadic Fixations When Doing the Visual Search Task

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PURPOSE. Individuals with amblyopia are known to have functional vision deficits (e.g., reduced reading speed) in spite of good visual acuity in the nonamblyopic eye. We studied and compared eye movements in children with and without amblyopia to examine how a visual scene is explored during visual search.

METHODS. Children (six to 16 years of age) in the control group ($n = 14$) and cases group with anisometropic amblyopia ($n = 23$) participated in a visual search study, in which they looked for targets in real-world images displayed on a computer monitor. Eyelink 1000 Plus was used to track the eye movements. Three viewing conditions were randomized: dominant/fellow eye, nondominant/amblyopic eye, and binocular viewing. Visual search performance was measured by combining search time and accuracy.

RESULTS. As expected, poorer visual search performance was observed in the amblyopic eye when compared to the controls and fellow eye ($P < 0.005$). However, the reaction time was longer even in binocular and fellow eye viewing conditions than the controls ($P < 0.028$). Children with amblyopia made more saccades (17 vs. 12, $P = 0.007$), without the need to fixate longer ($P = 0.312$), but with more fixations in the target interest area (4.65 vs. 3.14, $P = 0.002$) when compared to controls. These eye movement patterns were observed in both the fellow eye and binocular viewing conditions.

CONCLUSIONS. In spite of good visual acuity in the fellow eye, children with amblyopia needed to sample the scene with more fixations. Even upon gazing at the target location, they made more fixations before confirming a hit. These search patterns suggest a possible narrower spatial visual span to process the visual information in children with amblyopia.

Keywords: anisometropia, amblyopia, visual search, children

Amblyopia is characterized as a neurodevelopmental disorder of the visual system that results in poor visual acuity. The condition can be unilateral or bilateral. Unilateral amblyopia is clinically identified by visual acuity difference of two or more lines between the eyes. The most common cause of unilateral amblyopia is the onset of anisometropia or strabismus or both during visual system development in early childhood that was not intervened.¹ Because of the good visual acuity in the fellow eye, unilateral amblyopia condition is usually not classified as visual impairment.² A fair assumption is made that individuals with unilateral amblyopia can function normally in real-world conditions. However, research evidence demonstrates that may not be so. Even with binocular viewing, reading rate is found to be slower³ and deficits have been observed in image perception.⁴ Fixation instability,^{3,5,6} decreased visual span,³ lack of binocular summation,^{4,6,7} higher-order cortical deficits,⁸ and attentional deficiencies^{8,9} are some reasons attributed to the relatively poor performance in individuals with amblyopia. Taken together, individuals with amblyopia can have functional

vision difficulties even with fellow eye or binocular viewing conditions.^{6,10,11}

Functional vision is the use of vision for daily living activities. Functional vision can be measured by tasks that are closer to our daily activities (e.g., searching for a spice jar). Visual search has been used to assess functional vision in children and adults with visual impairment.^{4,8,12,13} A study done on adults with amblyopia using non-natural targets (Gabor patches) showed that subjects with amblyopia took longer search time only for the conjunction visual search and not for the feature search task, indicating that tasks requiring feature binding and higher cognition inputs can be impaired in amblyopia.⁸ Natural targets or real-world images are, however, more complex and can be representative of realistic scenes. Performing visual search with such images in naturalistic eye movement viewing condition can more closely correlate to real world functional vision tasks.

It has also been shown that patients with amblyopia have eye movement deficits.^{3,5-7,12,14,15} Specifically, fixation instability has been shown in these patients when eye movements were restricted, and attention was studied when performing

a search task.^{8,9} It is unclear what eye movement deficits will be noticed in a naturalistic and unrestrained viewing condition. Eye movement tasks such as visual search, will comprise of saccades and fixations. We hypothesized that patients with amblyopia having visual search deficits may show a different pattern of eye movement search that will be reflected in the saccades and fixations. If the search time is to be longer in amblyopia, it could be due to more fixations or longer fixation duration. We undertook a study to investigate these eye movement patterns in children with and without amblyopia.

METHODS

A prospective cross-sectional study was conducted. The Institutional Review Board of L V Prasad Eye Institute approved the study protocol, and the data collection was carried out in accordance to the tenets of Declaration of Helsinki. Children within the age group of six to 16 years were recruited from L V Prasad Eye Institute, Hyderabad, India. Written informed consent was obtained from the parents, and verbal assent was obtained from the children to participate in the study.

Participants

Children with established diagnosis of anisometric amblyopia, as per their medical records were enrolled into the cases cohort. These children were using their refractive correction for at least a period of four months and were included if their best-corrected visual acuity was 20/100 or better in the amblyopic eye, and 20/25 or better in their fellow eye. The visual acuity cut off of 20/100 was determined based on the ease to do the visual search task in a pilot study. Anisometropia was defined as refractive error difference in spherical equivalent between the two eyes to be 1.50 diopters or greater. Amblyopia was defined as difference in best-corrected visual acuity between the two eyes to be equal to two lines or greater. Patients with strabismus or any other pathology were excluded. Age-similar controls with best-corrected visual acuity of 20/25 or better in each eye were also recruited. Children of the employees in the institute or children visiting the institute for regular eye checkup were enrolled for the control group. All participants performed the experiment with their habitual spectacle correction, if any.

Visual Search Experiment

The visual search experiment used in this study was similar to those reported earlier.^{13,16,17} Essentially, images of real-world scenes that comprises of faces (e.g., group picture of a sports team), indoor scenes (e.g., kitchen), and collections of objects (e.g., bunch of flowers) were displayed on a computer monitor (18.5" HP W1972a monitor; Intel core i3-2120 CPU @ 3.30 GHz, 6 GB RAM, 1366 × 768 pixels). Along with this image, a "search target", selected from within the image was displayed at the top left corner of the monitor. The participant was instructed to find this search target within the displayed image as quickly and as accurately as possible, and then click on it with a computer mouse. The size of the search area was 16.2° × 29° (height × width). The size of the visual search target ranged from 1.2° to 8.9° in height and 0.9° to 7.8° in width. These visual search images were standardized to have comparable levels



FIGURE 1. Experimental set up, showing the eye tracker and the display monitor. The two Interest Areas (IA) are marked in the search image. The actual experiment was done in a dark room.

of difficulty.^{16,17} A buffer zone of 0.5° was provided around the search target (see also Eye tracking below, for additional details). A click anywhere within this buffer zone was considered to be an accurate trial.

Three viewing conditions were randomized for all the children. These viewing conditions were: performing the visual search task with the dominant eye (DE) (for controls) or fellow eye (FE) (for cases) and with the non-dominant eye (NDE) (for controls) or amblyopic eye (for cases) and binocular viewing condition (BE) (for both controls and cases). Each viewing condition had 30 trials, thus a total of 90 trials were presented for each participant. Dominant eye for the control children was decided based on the hole-in-the-hand method, a variation of the Miles test.¹⁸ The actual experiment began after giving nine practice trials to the children in the binocular viewing condition and ensuring they understood the task. Images used in practice trials were not shown in the main experiment. The experiment was carried out in a dark room.

Eye Tracking

The Eyelink 1000 Plus eye tracker (SR Research Ltd., Ottawa, Canada) was used for measuring the eye movements during the experiment. The tracker locates the first Purkinje image and the dark pupil, to compute the eye movement. The sampling rate was set at 500 Hz, except for six children in the control group and one child in the amblyopia group, where sampling rate was 250 Hz. The presented search images on the display monitor were synched with the eye tracker system and the recordings were coded using the Matlab program (MATLAB R2014b; Mathworks, Natick, MA, USA) and Psychtoolbox software.¹⁹⁻²¹ The participant sat in front of the display monitor with their head stabilized over a table-mounted head and chin rest in line with the eye tracker at a distance of 81 cm from the display monitor (Fig. 1). Depending on the viewing condition, both eyes or the tested eye was tracked. The nontested eye was patched. Eye tracking data of the dominant eye (in controls) or the fellow eye (in the amblyopia group) were extracted when the experiment was performed binocularly. A nine-point calibration and validation were performed at the beginning of each viewing condition. A drift correction was given after 20 trials to ensure

accuracy for eye movement measurements. Participants were given a break, if desired, during the drift correction.

Data Analysis

The outcome parameters from the visual search performance experiment included accuracy of the click, calculated in percentage, the total search time (reaction time) taken to identify and click the search target, and an integrated performance measure that accounts for time-accuracy trade-off. Essentially, the integrated search performance score was calculated by ordering the correct trials by reaction time to calculate the accumulative search speed and divide it by the time taken till then. Such a calculation captures the trend of slowing down, when the target difficulty increases. Higher the score better is the performance.¹³ Only those trials with accurate responses were considered for analysis. The outcome parameters from the eye tracker extracted through Eyelink's Data Viewer includes saccade count (total number of saccades made in the trial), saccade amplitude (average size in degrees of visual angle, of all the saccades in the trial), and fixation duration (average duration of all the fixations in a given trial). Additionally, two interest areas (IA) were marked (Fig. 1) that included the search target displayed at the top left of the display (IA1) and the actual position of the search target in the real world image (IA2). Within these interest areas the following eye movement parameters were extracted: refixation count (number of refixations to the same interest area, denoted as run count in the software), fixation count (number of fixations made in the interest areas) and average dwell time (average fixation durations in the interest areas). Data were analyzed using SPSS Statistics version 21 software (IBM Corp., Armonk, NY, USA). Mean \pm standard deviation values were reported. As each participant was tested in all three viewing conditions, and with two groups (controls and cases) to compare, repeated-measures ANOVA (RM-ANOVA) was performed with two subject groups as between-subjects factor and the three viewing conditions as within-subjects factor, with Bonferroni adjustment for multiple comparisons. $P \leq 0.05$ was considered as significant. Effect sizes were reported with the partial eta squared values (η^2p), values > 0.14 indicate significantly larger effect size.

RESULTS

A total of 40 children were enrolled for the study. Of this, three children with amblyopia were excluded because one could not be calibrated with the eye tracker, and for two others the parents wanted to discontinue the study in the middle because of lack of time. The demographic and visual

TABLE. Profile of the Participants (Mean \pm Standard Deviation Values Are Tabulated for the Two Groups)

	Controls	Children With Amblyopia
Number of participants	14 (5 males)	23 (9 males)
Age (yr)	10.57 \pm 3.34	10.91 \pm 2.89
Interocular logMAR visual acuity difference	0.00 \pm 0.0	0.36 \pm 0.14
Stereoacuity (log arc seconds)	1.52 \pm 0.22	2.22 \pm 0.60

parameters of the remaining children are shown in the Table. With the exception of four children, the rest of them were on patching therapy for amblyopia (see Supplementary Table S1 for additional details). All of the children were able to perform the task in all the test conditions, except for one participant (six years old/male) in the control group, who discontinued the study because of boredom in the last viewing condition (nondominant eye). This participant's data were included for the analyses of dominant/fellow eye and binocular viewing conditions and was excluded for other analyses that involved all the three viewing conditions. The total testing time for a participant was about 30 minutes. Mean age (Independent t test, $P = 0.744$) and the dominant eye visual acuity (independent t test, $P = 0.083$) were comparable between the groups.

Visual Search Performance

In spite of comparable visual acuity between the dominant and fellow eyes of the two groups, the overall visual search performance was poorer in the amblyopia group, with the difference being either significant (accuracy, $F[1,34] = 6.327$, $P = 0.017$, $\eta^2p = 0.157$; reaction time, $F[1,34] = 9.277$, $P = 0.004$, $\eta^2p = 0.214$) or tending toward significance (integrated search performance, $F[1,34] = 4.050$, $p = 0.052$, $\eta^2p = 0.106$, Fig. 2c). Interaction between the viewing conditions and the subject groups for accuracy was significant ($F[1,68] = 4.715$, $P = 0.016$, $\eta^2p = 0.122$). However, interaction effect was not present for the reaction time ($F[1,68] = 2.162$, $P = 0.130$, $\eta^2p = 0.060$) and integrated search performance score ($F[1,34] = 2.993$, $P = 0.057$, $\eta^2p = 0.081$).

As expected, post hoc analyses showed that the visual search performance (accuracy and integrated search performance score) for the amblyopic eye was poorer when compared with the fellow eye ($P < 0.001$) and with the nondominant eye of the control group ($P \leq 0.008$) (Fig. 2a). The reaction time of the amblyopic eye was also slower when compared to the nondominant eye of the control

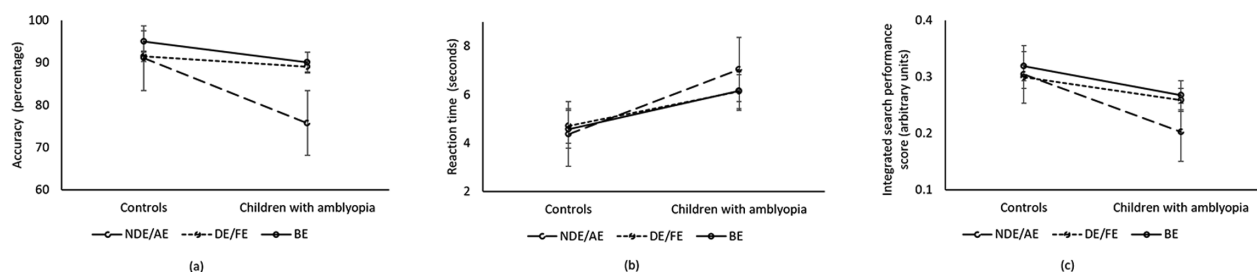


FIGURE 2. Line graphs showing the mean and standard error of mean for (a) accuracy and (b) reaction time and (c) integrated search performance scores for all the three viewing conditions in the two groups of participants. NDE: Non-Dominant eye, AE: Amblyopic eye, DE: Dominant eye, FE: Fellow eye and BE: Both eyes.



FIGURE 3. Example of visual search eye movements for an indoor image made by (a) a control participant and (b) a participant with amblyopia during the binocular viewing condition. Fixations are shown in circles, and saccadic trajectories are shown as arrow lines.

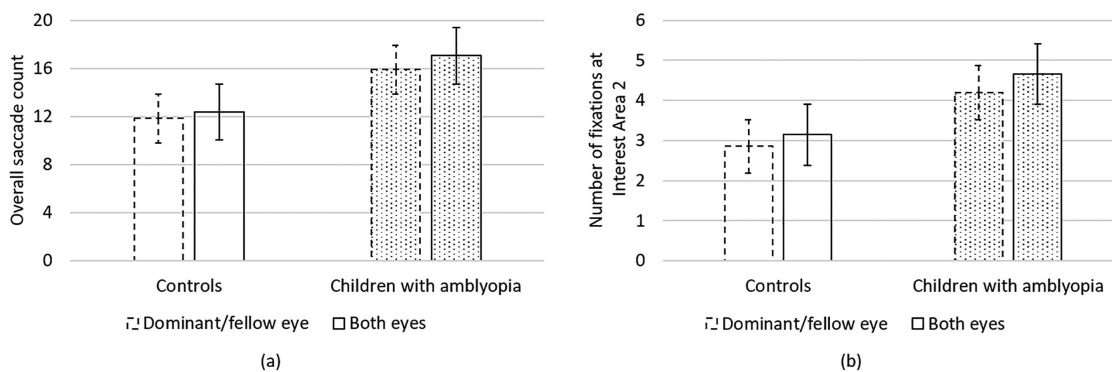


FIGURE 4. Mean \pm standard error of mean of (a) the overall saccade count and (b) number of fixations in the Interest Area 2 (target location) of dominant/fellow eye and both eyes of controls (white box) and children with amblyopia (dotted box).

group ($P = 0.002$). In within group comparison, the reaction time of the amblyopic eye was significantly longer in the binocular viewing ($P = 0.013$) and in the fellow eye ($P = 0.046$) viewing condition (Fig. 2b).

With increase in age there was a significant improvement in visual search performance for the control group (Pearson's correlation, $r = 0.702$, $P = 0.005$), whereas such a correlation appeared to be relatively weaker in children with amblyopia (Pearson's correlation, $r = 0.514$, $P = 0.012$). However, the correlation between the two groups was not significantly different (Fisher's r -to- z -transformed, $P = 0.419$, $Z = 0.807$). No correlation was observed between the binocular integrated performance score and interocular visual acuity difference or stereoacuity of children with amblyopia (Pearson's correlation, $P \geq 0.732$).

Because differences in the amblyopic eye were obvious and could cause significant difference between the two groups in the model, further results reported here for eye movements focus on the analysis performed between the two groups only for the binocular and dominant/fellow eye viewing conditions (also see Supplementary Table S2).

Children with amblyopia made significantly more number of saccades ($F[1,35] = 8.33$, $P = 0.007$, $\eta^2p = 0.192$) in the fellow/dominant eye (FE vs. DE: 15.89 ± 4.78 vs.

11.82 ± 3.09) and under binocular viewing condition when compared to the control group (17.04 ± 6.85 vs. 12.36 ± 2.96) (see also Figs. 3, 4a). This trend was reflected in the number of fixations as well, and the results were similar to that reported for saccades. Saccadic amplitude under binocular viewing of children with amblyopia appeared smaller (amblyopia vs. controls: FE vs. DE: $4.58^\circ \pm 0.92^\circ$ vs. $5.09^\circ \pm 0.51^\circ$, Binocular: $4.58^\circ \pm 1.21^\circ$ vs. $5.28^\circ \pm 1.4^\circ$) than children in the control group but didn't reach statistical significance ($F[1,35] = 4.05$, $P = 0.052$, $\eta^2p = 0.104$). Between the two groups, the average fixation duration was comparable ($F[1,35] = 1.05$, $P = 0.312$, $\eta^2p = 0.029$), but there was a significant interaction ($F[1,35] = 5.94$, $P = 0.020$, $\eta^2p = 0.145$) between the viewing conditions and the subject groups, with duration being comparable in the binocular viewing condition but not between the fellow and dominant eye viewing condition (Amblyopia vs. Controls: FE vs. DE: 291.41 ± 58.64 vs. 323.96 ± 49.63 ; Binocular: 284.78 ± 50.64 vs. 286.14 ± 45.96). Within the control group, children fixated for a shorter duration through binocular viewing when compared to the monocular viewing conditions ($P \leq 0.008$). However, in the amblyopia group, the duration was comparable through the fellow eye and binocular viewing, indicating that there was no binocular advantage ($P = 0.910$).

Fixations and refixations were comparable between the two groups for the first interest area, which is the search target displayed on the upper left corner (Fig. 1, IA1). However, eye movements of the two groups differed in the second interest area (Fig. 1, IA2), which is the actual target area within the image. Essentially children with amblyopia made significantly ($F[1,29] = 0.031$, $P = 0.002$, $\eta^2p = 0.287$) more fixations in the second interest area, in both the fellow eye (2.85 ± 0.92 vs. 4.19 ± 1.54) and binocular viewing conditions (3.14 ± 0.88 vs. 4.65 ± 2.09) (see also Figs. 3, 4b).

DISCUSSION

This study showed a reduced visual search performance in children with anisometropic amblyopia when compared to their normally sighted peers. This reduction was present in spite of viewing binocularly, with their fellow eye having good visual acuity. The reduced performance in children with amblyopia was a consequence of taking a longer time (1.57 seconds longer, factor of 1.3) (Fig. 2b, also see Supplementary Table S2) to perform the visual search task, albeit with comparable accuracy as the normally-sighted children (Fig. 2a). The longer reaction time taken to accomplish the search task was further investigated by analyzing the eye movement parameters. It was observed that children with amblyopia made more saccades and fixations (Fig. 4a), a trend that was significant in all the three viewing conditions, when compared with normally-sighted children. More importantly, they have made more fixations, particularly to the target interest area (IA2), to confirm that it was indeed the target (Fig. 4b). These main findings are discussed below.

Although poor visual search performance in the amblyopic eye can be explained by the limitation in visual acuity, a decrease in performance even in the fellow eye either independently or in binocular viewing, indicates visual acuity alone cannot explain this visual search performance deficiency. In fact, the search performance was poorly correlated to the interocular visual acuity difference, indicating that visual acuity may not fully predict functional performance in a task such as visual search as used in this study. The findings of decreased performance in binocular/fellow eye are in agreement with previous studies^{8,9} that have also investigated visual search in individuals with amblyopia. In those studies, the performance deficits were speculated to rise from higher-order visual processing skills that included attentional and perceptual factors. The increased reaction time in visual search task has also been observed in both the amblyopic and dominant eye of individuals with amblyopia.^{8,12} The increased reaction time in binocular viewing conditions was also shown in a recent study⁹ that investigated visual attention. The reasons accounting for the longer search time can be uncovered by investigating the eye movement patterns. Some of the eye movement outcomes from this study were robust in that a similar pattern was observed in both the binocular and fellow eye viewing condition.

Eye movements in visual search tasks comprises of saccades and fixations. To plan and execute an effective search, a minimal number of saccades with minimal fixation duration, without having the need to re-examine the same search area (regression saccades or refixations), should be used. In this study, we observed that the fixation duration was comparable between the two groups. However, the main difference was that children with amblyopia needed more fixations for examining the targets. This resulted in more eye movements and thus longer time to identify the

target. A similar pattern of increased saccades and fixations has been found in a study³ that investigated reading performance in children with amblyopia. In that study, it was speculated that the saccades were undershooting the preferred landing position. This speculation may not explain the finding in the present search study, in which the location of the target is the preferred position to land. What we show is that children with amblyopia already landed their gaze points on the targets, but they could not confirm it right away. Sometimes they made more subsequent fixations within the target area, and sometimes they checked outside the target area and then went back to it (See example in Fig. 3b).

We explain the findings using the visual span concept, which is defined in this study as the amount of visual information taken in one fixation.²² Although the time taken for visual processing (fixation duration) is comparable, the amount of information taken, in one fixation by the amblyopic system is perhaps inadequate in comparison to the visual information taken by a normal visual system with one fixation. This might create the need for the amblyopic system to make more saccades and fixations to gather the same amount of information that the normal system obtains with fewer saccades and fixations. This narrower visual span in amblyopia might also be a way to compensate for the visual crowding reported in the amblyopic visual system.²³ A decrease in crowding has been observed with an increase in visual span after training individuals with amblyopia in a perceptual learning task.²³

Fixation instability and inaccurate saccades in amblyopia may increase the regression saccades. However, in the present study, largely such a trend was not observed, by analyzing the refixation count in the interest areas. This finding is in agreement to the reading study³ that did not show higher regressive saccades. We did not look at the refixation saccades outside the interest areas. However, we found that children with amblyopia have made a greater number of fixations outside the interest areas when compared to the control group (Supplementary Table S2). This might indicate the difficulty that children with amblyopia had, to quickly localize to the target, which created the need for them to make multiple fixations. These children also had smaller saccadic amplitude when compared to the control group (although only tending towards statistical significance, $P = 0.052$). These smaller amplitude saccades could have resulted either from their fixation instability, requiring a need to make smaller refixatory saccades. It has been found that microsaccades in children with amblyopia are less frequent.¹² It is possible that these fine tuning microsaccades are instead replaced by these relatively small amplitude saccades. We analyzed the microsaccades under binocular viewing using the Engbert and Kliegl Algorithm.²⁴ We observed a similar trend in that the frequency of the microsaccades was lesser in children with amblyopia ($0.97 \text{ Hz} \pm 0.37$) when compared to the control group ($1.19 \text{ Hz} \pm 0.48$); however, this trend was not significant ($P = 0.193$).

Saccadic latency is known to be longer in amblyopia with more number of corrective saccades.⁷ The task used in this study did not have a single localizing target to study latency or corrective saccades; hence, latency calculation was not appropriate. Instead, the total search time taken (reaction time) to complete the task was computed. Whether small amplitude saccades can be seen as corrective saccades cannot be commented upon in this study with real-world images, because it will not be clear if, in general, an exploratory small eye movement was made to the objects in

the image or if truly a corrective saccade was made toward the target that the participant intended to investigate. Additionally, hypometric saccades are common in children when compared to adults.²⁵ It is possible that in amblyopia, the saccade amplitude calibration is still immature, leading to smaller-amplitude or hypometric saccades in comparison to their peers. Bilateral inputs are needed to curate the development of eye movements, particularly vertical directions and an early monocular visual loss can affect these eye movements.²⁶

In cases of amblyopia, one could speculate binocular inhibition^{6,27} if there was a decrease in performance under binocular viewing conditions when compared to monocular viewing condition. In the present study the performance score and the reaction time in children with amblyopia were similar in both binocular viewing and fellow eye-viewing conditions, negating the binocular inhibition argument. Also, in the controls group no improvement in performance was observed under binocular viewing condition, thus indicating no binocular summation advantage in the given visual search task. In an earlier study from our group, we observed an improvement in visual search performance with increase in age.¹³ This trend was observed in the control group but not for children with amblyopia in this study. The latter group may have a similar disadvantage like other children with low-vision conditions, who also did not show the age dividend.¹³ It may be interesting to recruit older participants with amblyopia as well, to see if this disadvantage continues or if it is remediated at a later time.

In conclusion, this study shows that children with amblyopia can have functional vision difficulties even when performing a task binocularly. This was demonstrated through a reduced visual search performance using real-world images. The implication of this result can be for patching/vision therapy given for amblyopia management. In typical therapy exercises for amblyopia, a battery of goal-oriented tasks such as visual memory, saccades, and more are given. The evidence or the scientific basis for including these exercises has never been well established. Our study show there could be deficiencies in a goal-oriented performance task in children with amblyopia. The study also highlights that both the amblyopic eye and the fellow eye show deficiencies. Hence, training both the eyes might need to be considered in amblyopia. We did not investigate the role of patching therapy in the visual search performance of children with amblyopia in this study. We plan to take eye movement measurements before starting patching/vision therapy and to reevaluate the eye movement parameters after the therapy to observe for a change or improvement in these parameters, if any.

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