Effectiveness of a Novel Video Game Platform in the Treatment of Pediatric Amblyopia

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ABSTRACT

Purpose: To test the non-inferiority of a novel game platform for the treatment of pediatric amblyopia compared to standard eye patching.

Methods: Forty participants (ages 4 to 18 years) across seven optometric clinics in the United States diagnosed as having amblyopia associated with anisometropia were randomly assigned to either 12 weeks of eye patching therapy (n = 19) or Barron Vision (Barron Associates, Inc) video game treatment (n = 21). Participants in the eye patching group with best corrected visual acuity (BCVA) worse than 20/200 in their amblyopic eye were prescribed 6 hours of patching daily, whereas those whose BCVA was 20/200 (1.00 logarithm of the minimum angle of resolution [logMAR]) or better were instructed to patch for 2 hours daily. Participants in the video game group, irrespective of the severity of their amblyopia, were instructed to play four different 5-minute mini-games five times a week for a total of 20 minutes a day.

Results: A mixed linear modeling analysis of before and after BCVA differences after 12 weeks showed the non-inferiority of video game treatment to eye patching using a 0.10 logMAR threshold while adjusting for the participant's age, sex, and baseline BCVA.

Conclusions: The results of the study suggest that a 12-week home-based video game vision therapy intervention can provide equivalent treatment outcomes to eye patching for amblyopia in children ages 5 to 18 years. Video game–based vision therapy may be a more acceptable and time-efficient alternative to existing approaches. By incorporating elements of perceptual learning, approaches such as Barron Vision video game treatment may have additional long-term therapeutic benefits and may improve treatment compliance.

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INTRODUCTION

Pediatric amblyopia is the leading cause of monocular visual impairment, affecting between 1.3% and 3.6% of children globally.[1] Traditionally, it has been considered a monocular disorder that can be effectively treated by patching the sound eye, thereby strengthening the functionality of the amblyopic eye. When complied with, this procedure has been reported to improve visual acuity for 73% to 90% of children with amblyopia.[2,3] At the same time, normal visual acuity may not be achieved in as many as 50% of children with amblyopia treated for a prolonged period of time.[4] Furthermore, some studies suggest that amblyopia recurrence after successful treatment may affect between 25% and 50% of children.[5] A randomized trial of treatment of amblyopia in children aged 7 to 17 years showed that 2 to 6 hours of daily patching with near activities was most effective

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for patients between 7 and 12 years old, even if the amblyopia had been previously treated.[6] At the same time in patients 13 to 17 years old, addition of daily patching between 2 and 6 hours with near activities was of little benefit if amblyopia had previously been treated with patching. The new American Academy of Ophthalmology Amblyopia Preferred Practice Pattern similarly provides a discretionary provision that patching could still be considered for older children and teenagers, especially if they have not previously been treated.[7] Additionally, both Monitored and Randomized Occlusion Treatment of Amblyopia Studies showed that compliance with patching treatment averages less than 50% of the prescribed time,[3,8] making it a suboptimal treatment method.

In more recent studies, an argument has been made about the utility of binocular treatment approaches to pediatric amblyopia treatment. Several groups compared the effectiveness of eye patching with video game–based contrast rebalancing that allows the child to overcome interocular suppression and experience binocular vision while playing the games. In these studies, children wore red-green anaglyphic glasses that separated game elements seen by each eye, so that reduced-contrast elements are seen by the fellow eye, high-contrast elements are seen by the amblyopic eye, and high-contrast background elements are seen by both eyes. Amblyopic eye contrast remained at 100% contrast, whereas fellow eye contrast was gradually increased, placing greater demands on the amblyopic eye to work as a team with the sound eye.

However, this approach has yielded mixed results. For example, Kelly et al[9] showed that this binocular game approach was more effective than patching after 2 weeks of treatment in improving best corrected visual acuity (BCVA) and depth of suppression. Similarly, Jost et al[10] recently demonstrated that the contrast rebalancing approach applied to dichoptic movies may be particularly suitable as a home treatment for young children (between 3 and 7 years old) with amblyopia, who in their study showed excellent compliance and a high degree of motivation to comply with the treatment. At the same time, Gao et al[11] did not find a difference between contrast-based video game treatment and a placebo group video game treatment that did not manipulate contrast between the eyes after 6 weeks of intervention. Moreover, Kelly et al[9] and Jost et al[10] only tested young children, whereas Gao et al[11] had a much wider age range between 7 and 55 years. The latter group concluded that they did not find sufficient evidence of the causal role of suppression in the etiology of amblyopia.

In the current study, we compared the utility of a novel, low-cost video game platform, Barron Vision (Barron Associates, Inc), with standard eye patching in the treatment of pediatric amblyopia. Unlike previous gaming studies, our platform used a monocular perceptual learning approach to amblyopia treatment. Recent evidence suggests that monocular perceptual training not only results in improvement of monocular function in the amblyopic eye, but also transfers to benefit binocular function.[12] In the Barron Vision platform, the size of optotypes is manipulated and presented to the amblyopic eye at the limit of its visual acuity while completely suppressing these optotypes from the sound eye through a cyan lens of anaglyph glasses. Special fiducials integrated into the frame of the anaglyph glasses were used for automatic tracking of the distance of the participant from the screen. Changes in distance triggered corresponding adjustments of the size of the optotypes, thereby ensuring treatment fidelity. This stimulus manipulation was incorporated into a series of mini-games. The current study included the full age range of pediatric participants (from 5 to 18 years old) and used the standard 12-week protocol typically conducted with eye patching.[6] We hypothesized that participants in the video game group would show similar improvements in BCVA (ie, be non-inferior to) as the eye patching group, but with minimal time investment, and therefore maximal efficiency. The motivational aspect of the gaming experience was also hypothesized to improve treatment compliance.

PATIENTS AND METHODS

Participants

All study procedures including participant recruitment, treatment, and data analyses were approved by the Institutional Review Board of the University of North Dakota. Participant recruitment was carried out by seven optometric clinics across the United States within their serviced communities. Using each practice's patient database and going back to 2 years of patient records, participating providers were asked to identify up to 5 pediatric patients with diagnosed amblyopia who satisfied the study criteria below.

Inclusionary criteria included age between 4 and 18 years, diagnosis of amblyopia associated with

TABLE 1

Demographic Characteristics of the Sample

Variable	Eye Patching (n, %)	Video Game (n, %)	Analysis	*P*
Age, years			19.62[a]	.11
5 to 7	6 (31.6)	8 (38.1)		
8 to 10	5 (26.3)	3 (14.3)		
11 to 13	5 (26.3)	3 (14.3)		
14 to 16	2 (10.5)	6 (28.6)		
17 to 18	1 (5.3)	1 (4.7)		
Sex			0.42[a]	.52
Male	8 (42.1)	11 (52.4)		
Female	11 (57.9)	10 (47.6)		
Race			6.0[a]	.42
American Indian/Alaskan Native	0 (0)	1 (4.8)		
Asian	1 (5.3)	0 (0)		
Black/African American	0 (0)	1 (4.8)		
More than one race	1 (5.3)	0 (0)		
Native Hawaiian/Pacific Islander	1 (5.3)	0 (0)		
White	16 (84.2)	17 (85.0)		
Not reported	0 (0)	2 (9.5)		
Amblyopic eye			0.63[a]	.43
Right	14 (73.7)	13 (61.9)		
Left	5 (26.3)	8 (38.1)		
Acuity in the amblyopic eye at baseline (logMAR), mean ± SD	0.52 (0.27)	0.56 (0.19)	-0.55[b]	.58

logMAR = logarithm of the minimum angle of resolution; SD = standard deviation
[a]Chi-square test.
[b]*t* test.

anisometropia (see definition below), no amblyopia treatment (atropine, patching, Bangerter, or vision therapy) in the preceding month, use of glasses (if required) for at least 16 weeks, or demonstrated stability of visual acuity (< 0.1 logarithm of the minimum angle of resolution [logMAR] change by the same testing method measured on two examinations at least 4 weeks apart), visual acuity in the amblyopic eye of 20/40 or worse (≥ 0.30 logMAR), visual acuity in the fellow eye of 20/25 or better (≤ 0.10 logMAR), and interocular difference of 0.3 logMAR or greater (3 logMAR chart lines).

Refractive/anisometropic amblyopia was defined as amblyopia in the presence of anisometropia of 0.50 diopters (D) or greater in spherical equivalent or 1.50 D or greater of difference in astigmatism in any meridian, with no measurable heterotropia at distance or near fixation, which persisted after at least 4 weeks of spectacle correction.

Exclusionary criteria included the use of prisms in the refractive correction at the time of enrollment, previous intraocular or refractive surgery, any form of treatment for amblyopia in the past month, diagnosis of Down syndrome or cerebral palsy or other severe developmental delay that could interfere with treatment or evaluation, or heterotropia or heterophoria with a total ocular deviation greater than 10 prism diopters at near.

Forty-nine participants were recruited for the study and were randomly assigned to either the eye patching (n = 23) or video game (n = 26) groups. Of these, 40 participants (81.6%) went on to complete the prescribed 12 weeks of vision therapy and associated assessments (19 participants in the eye patch-

ing group and 21 in the video game group). These 40 patients ("completers") represented the analytical cohort with respect to all visual acuity–related data analyses. Twenty-one of the completers were female (52.5%) and 19 were male (47.5%). Their ages ranged from 5 to 18 years. They were predominantly White (n = 37). The demographic characteristics of the sample are presented in **Table 1**.

Materials

Barron Associates, Inc developed the Barron Vision gaming software system to support vision therapy for individuals with non-strabismic amblyopia. The software was installed on a third-party media playing device (Nvidia Shield) connected to an ASUS VK228H widescreen (21.5" W) high-definition (1,920 × 1,080) LCD monitor with an in-build HD webcam. The software was operated using an 8Bitdo SF30 Pro game controller, connected to the Nvidia Shield.

The Barron Vision software incorporated ten 5-minute mini-games that all required recognition and discrimination of appropriately sized optotypes to be successful in the activities. The games included matching exercises, character recognition, memory games, and arcade-style games. All games were completed while wearing special reversible red-cyan anaglyph glasses with the red lens placed over the amblyopic eye. The games involved recognition and discrimination of red target optotypes, whose size was based on the results of a short calibration activity (an optotype matching activity performed at the start of each session to estimate current visual acuity limit) and the distance of the participant from the screen. Distance from the screen was automatically estimated using webcam-based tracking of special markers (fiducials) integrated into anaglyph glasses worn by the player (**Figure 1**). Software used this estimated distance to adapt the size of presented optotypes, so if the player got closer (farther) to the screen, the optotypes became smaller (larger) based on this distance. Examples of amblyopia games are presented in **Figure 2**.

Three visual challenge levels were available. In the easy setting, optotypes were 0.4 logMAR larger in size than the estimated acuity limit determined by the calibration activity. In the medium setting, optotypes were 0.2 logMAR larger in size than the acuity limit. In the hard setting, optotypes were presented at the estimated limit of visual acuity. By default, all optotypes were set to medium. Additionally, optotype sizes were further automatically enlarged in games that incorporated additional visual challenges such as moving targets or high cognitive/attentional demand.

Figure 1. Barron Vision (Barron Associates, Inc) anaglyph glasses with tracking fiducials.

Completion of each daily session allowed players to access different portals of the Dragon Lair, an "Open World" that could be explored by a flying baby dragon for 10 minutes using stars earned during correct completion of mini-game targets. More difficult optotype levels earned more stars. The inclusion of this activity was intended to enhance the motivational aspect of treatment and further improve compliance. The Open World quest involved traversing expansive regions, which included a forest, volcanos, tundra, and mountains (**Figure 3**). The dragons could walk/run over land, fly in the air, and swim underwater while exploring spaces such as a giant "tree of life," volcanic caves, and underwater ice formations to find coins, special jewels, and puzzle pieces. To better succeed, the baby dragon had to grow and accumulate power by way of greater physical stature, stronger dragon breath, and faster movement/higher flying. All of these abilities were directly associated with the number of stars earned during completion of therapy games.

Procedure

Eligibility evaluation was conducted by participating optometrists under standard optometric practices. For children younger than 7 years, visual acuity in each eye was measured using isolated surrounded HOTV optotypes, whereas those 7 years and older were tested using the Early Treatment Diabetic Retinopathy Study (ETDRS) testing protocol

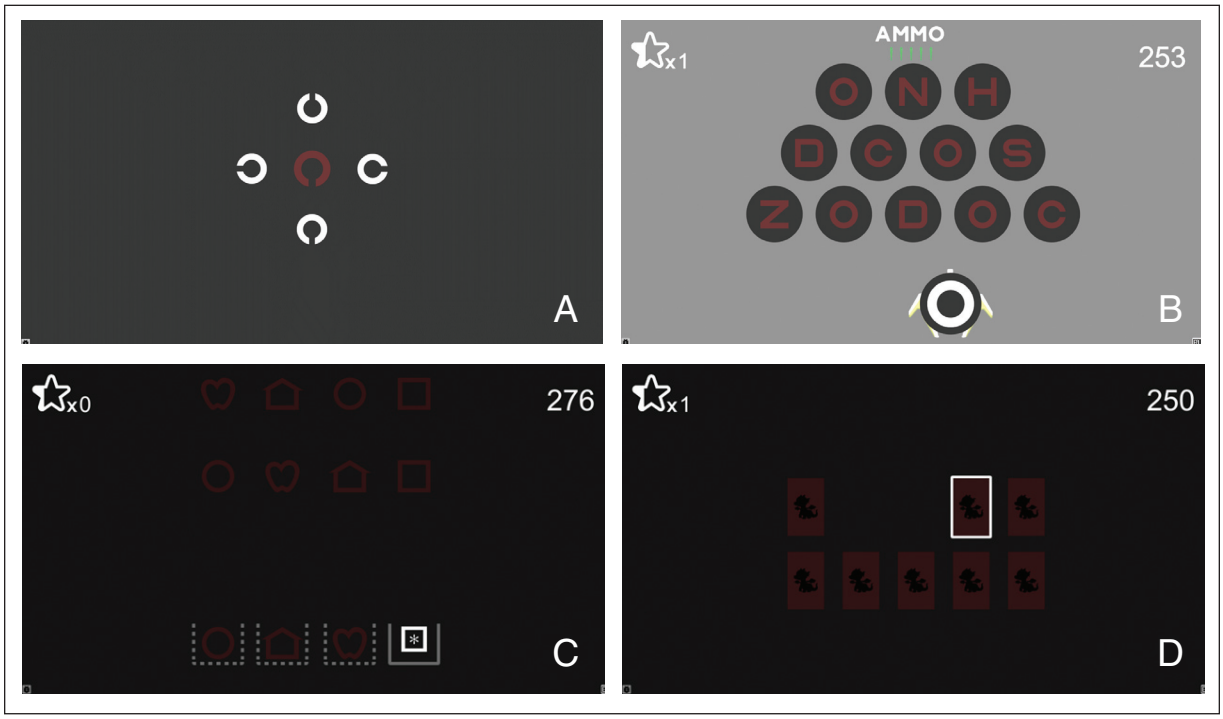

Figure 2. Examples of the calibration procedure and three amblyopia therapy games in the therapy mode (Barron Vision; Barron Associates, Inc): Shooting Stars, Egg Drop, and Concentration. (A) The task was to match the opening of the Landolt C with one of the four orientations (left, right, up, or down) and press the corresponding arrow on the game controller. The size of the optotype decreased with each successful attempt. (B) The object of the Shooting Stars game is to align the cannon with the same letter seen by the amblyopic eye in the rows of red stimuli as the letter embedded in the body of the cannon and then shoot the cannon to hit the matched letter. (C) The object of the Egg Drop game is to place a target shape or letter (white) into the basket that is vertically aligned with the same shape or letter dropping at a constant speed from the top within an array of distractors of varying size. (D) In the Concentration game, an array of letters is briefly shown to the participant, with duplicate letters in different positions on the screen. The letters are then covered by a dragon symbol, and the participant is asked to uncover matching pairs or triplets of letters using the game controller.

for visual acuity. Both protocols were based on the validation procedures used in the Pediatric Eye Disease Investigator Amblyopia Treatment Study with children.[13]

If the participant was found eligible and was interested in enrolling in the study, they were referred by the evaluating optometrist (ie, blinded examiner) to a vision therapist or another staff member (ie, unmasked examiner) at the clinic. The unmasked examiner was an investigator who carried out all consent procedures, assigned treatment, and conducted appropriate participant trainings. The participant was then randomly assigned to either the eye patching group or the video game group. If the participant was assigned to the eye patching group, they were reassured that they would also have an opportunity to experience the video games following completion of 12 weeks of study participation. The evaluating optometrist remained blind to the assigned treatment condition of the participant throughout the duration of the participant's participation in the study. Neither the therapist nor the participant (or their legal guardian) was allowed to discuss or mention their treatment condition to the blinded examiner.

If the participant was randomized into the eye patching group, the unmasked examiner trained the participant to perform eye patching procedures. Participants were provided with both adhesive skin patches and spectacle occluders that could be used interchangeably throughout the duration of the study. Participants with BCVA worse than 20/200 in their amblyopic eye were prescribed 6 hours of patching daily (covering the non-amblyopic eye), whereas participants whose BCVA was 20/200 (1.00 logMAR) or better were instructed to patch for 2 hours daily. Both participants and their guardians were instructed to make sure that the child spent at least 1 of the hours of patching time each day doing near-visual activities or other activities requiring eye–hand coordination. The instruction to perform 1 hour of near activities was identical in the 6-hour and 2-hour

patching groups. The participant/guardian was then given a home log form to complete, for which the duration of patching (in minutes) had to be indicated for each day of therapy. The guardian then received a full schedule of all in-person examinations and phone follow-up appointments. Follow-up examinations with the optometrist were scheduled after completion of 4, 8, and 12 weeks of therapy, respectively (±3 days for each assessment point). Phone follow-up appointments were conducted by the unmasked examiner every week to assess compliance with the treatment, answer questions, and motivate the participant to continue with the therapy.

At each follow-up visit, the participant's visual acuity was again assessed by the blinded examiner using the protocols described above. After each evaluation, the unmasked examiner then collected home log forms from the participant and completed a corresponding therapist form assessing treatment compliance and noting any issues.

If the participant was randomized into the video game group, the follow-up visit and contact protocols were identical to those used in the eye patching group above. During the initial office visit, the participant was trained by the therapist on how to use the Barron Vision system. The participant had to demonstrate the ability to access their user profile, complete a calibrating procedure ("Excalibrate") that marked the start of each daily session, and competently play at least two mini-games in the office before they could take the system home. Each participant, irrespective of the severity of their amblyopia, was instructed to play four different 5-minute mini-games at home five times a week for a total of 20 minutes a day. This session duration was chosen as a minimum effective dose consistent with other at-home vision therapy options, which typically specify anywhere between 15 minutes,[9] 30 minutes,[14] and 1 hour[11] of exercise per day, approximately 5 days per week. The participant's guardian was trained in how to set up the system and provided with technical support materials. The calibration exercise was completed at the beginning of each daily session to determine the appropriate visual challenge level for the games. The participant received a home log form to complete for 4 weeks before each follow-up visit. The form tracked the number of days each week the games were played, their names, and whether any of the games were played more than once. During each follow-up visit, the participant turned in the completed log form to the therapist and received a new one covering the next 4 weeks of treatment. The participant was asked to return the system at the time of their 12-week follow-up visit to the clinic.

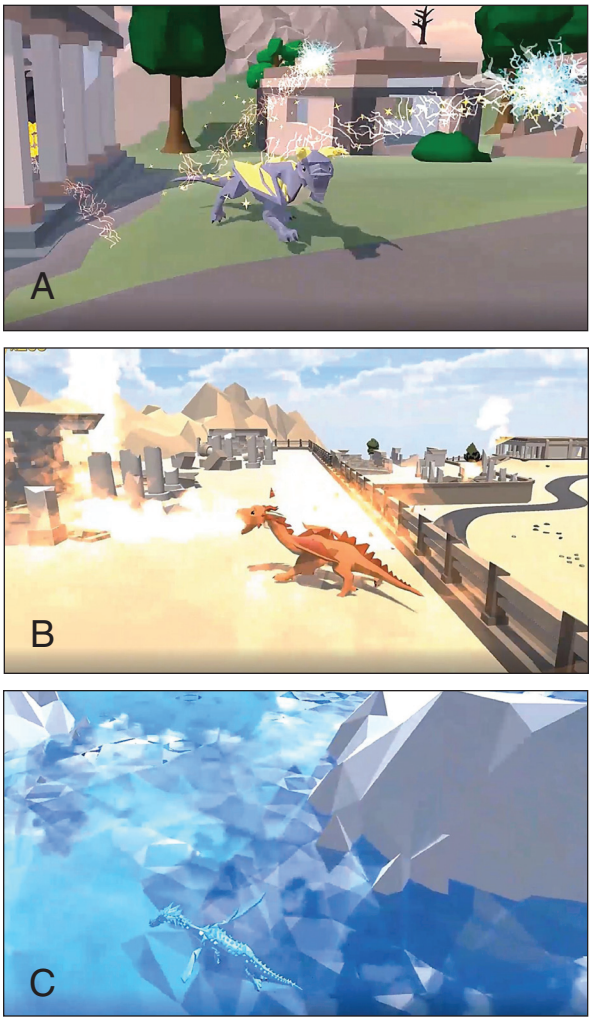

Figure 3. The Barron Vision Open World examples (Barron Associates, Inc), which included (A) forest, (B) volcano, and (C) mountain regions that could be explored by the player's baby dragon as a reward for completion of the therapy activities. There is no therapeutic component to this activity. It is designed to reinforce interest in the games.

Data Analysis

In our primary data analyses, we tested a non-inferiority hypothesis of video game treatment compared to eye patching. Specifically, we hypothesized that 12 weeks of Barron Vision video game therapy would result in significant improvement in visual acuity in both groups, so that that the mean 12-week change from baseline would be less than 0 in logMAR units (ie, $\Delta_{12\text{ weeks} - \text{baseline}} < 0$). Furthermore, we hypothesized that the visual acuity improvement in the video game group would not be inferior to the gain in acuity in the eye patching group. The non-inferior

TABLE 2

Cross-sectional Analysis of Visual Acuity (logMAR) Differences After 12 Weeks

Model Estimate	Parameter	Estimate	Upper 95% CL	Critical Threshold	*t*	*P* (T < t) Under-Ho	Reject: Ho
Within-group comparison							
Unadjusted							
Patching	$\Delta_{12\ weeks - 0\ weeks}$	-0.131	-0.019	0[a]	-2.25	.031[b]	Yes
Video game		-0.134	-0.023	0[a]	-2.35	.029[b]	Yes
Adjusted[c,d]							
Patching	$\Delta_{12\ weeks - 0\ weeks}$	-0.122	-0.011	0	-2.13	.038[b]	Yes
Video game		-0.133	-0.020		-2.34	.031[b]	Yes
Between-group comparison							
Unadjusted							
Patching	$\Delta_{video\ game} - \Delta_{patching}$	-0.003	0.093	0.10[e]	-1.82	.039[f]	Yes
Adjusted[c]							
Video game		-0.010	0.086	-1.93	0.031[f]	Yes	

CL = confidence level; logMAR = logarithm of the minimum angle of resolution

[a]Superiority.

[b]$\Delta_{12\ weeks - 0\ weeks} \geq 0$.

[c]Adjustment factors are age sex and pre-intervention visual acuity (ie, logMAR).

[d]Adjusted so that the control and intervention populations consist of children 10 years of age, half of whom were female and half of whom were male, and who all had pre-intervention visual acuity (logMAR) in the amblyopic eye = 0.54.

[e]Non-inferiority.

[f]$\Delta_{video\ game} - \Delta_{patching} \geq 0.10$.

visual acuity threshold was chosen a priori and defined as 0.10 logMAR units, which is equivalent to a one-line change on the Snellen visual acuity eye chart. Under this threshold, it was thus assumed that the 12-week change in visual acuity in the amblyopic eye in the video game group ($\Delta_{video\ game}$) would not be greater than 0.10 logMAR units compared to the 12-week change in acuity in the eye patching group ($\Delta_{patching}$). In symbolic notation that would be equivalent to $\Delta_{video\ game} - \Delta_{patching} < 0.10$ logMAR. Conversely, under the null hypothesis, it is assumed that $\Delta_{video\ game} - \Delta_{patching} \geq 0.10$ logMAR units. We also tested the same hypothesis at each assessment point, including 4 and 8 weeks of intervention. For each non-inferiority null hypothesis test, an a priori one-sided $\alpha = 0.05$ decision rule was used as the null hypothesis rejection criterion.

We used linear mixed modeling available in SPSS version 28.0 software (IBM Corporation) to test our primary cross-sectional non-inferiority hypothesis of visual acuity change at 12 weeks compared to baseline ($\Delta logMAR_{12\ weeks - 0\ weeks}$) between the two groups. In this model we entered intervention group as a fixed effect. Additionally, we adjusted for participant age, sex, and baseline visual acuity in the amblyopic eye by entering them as covariates in the model. Because our participants were nested within study sites (ie, clinics), we further specified study site and participants nested within study sites as random effects in the model. We used the restricted maximum likelihood method of estimation.

RESULTS

Primary Analyses

Our cross-sectional analysis of visual acuity differences before and after treatment showed that after 12 weeks of treatment, visual acuity was improved by -0.131 logMAR (upper 95% confidence level: -0.019 units, $P = .031$) in the eye patching group and by -0.122 logMAR (upper 95% confidence level: -0.011 units, $P = .038$) in the video game group. After covariate adjustment for patient age and sex and pre-intervention visual acuity, the null hypothesis that the video game eye therapy is inferior to the standard eye patching therapy was rejected ($P = .031$), suggesting non-inferiority of the video game treatment protocol to eye patching. Tabular and graphic summaries of the 12-week change in visual acuity are provided in **Table 2** and **Figure 4**, respectively.

Treatment Compliance

For all participants who completed the study, compliance data were estimated every 4 weeks as a percentage of the assigned treatment intensity. For eye patching, this percentage was determined by multiplying the average number of days per week during a 4-week period by the average number of minutes of daily patching and then dividing the product by 840 (for those with the 120 minutes per day treatment) or by 2,520 (for those with the 360 minutes per day treatment) and then multiplying the quotient by 100. For users in the video game group, the percentage was determined by multiplying the average number of days of game play per week during a 4-week period by the average number of games played per session during that period and then dividing the product by 20 and multiplying the resultant quotient by 100. The mean percentage of treatment compliance was then determined by averaging results for 4, 8, and 12-week follow-up visits, respectively. The mean "average relative compliance" was 79.5% (95% CI: 67.8 to 91.2%) for the eye patching group and 85.7% (95% CI: 78.1 to 96.8%) for the video game eye therapy group. This 8.0-unit difference (%) in mean average compliance (95% CI: -6.5 to 22.5%) was not statistically significant (P = .271).

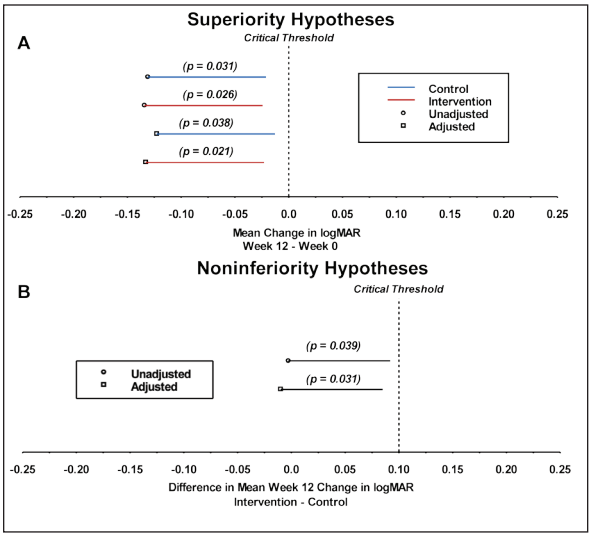

Figure 4. (A) The 12-week unadjusted and age, sex, and pre-intervention logarithm of the minimum angle of resolution (logMAR) adjusted superiority hypotheses one-sided 95% confidence intervals for the 12-week change in visual acuity and (B) the 12-week unadjusted and age, sex, and pre-intervention logMAR adjusted non-inferiority hypotheses one-sided 95% confidence intervals for the between intervention difference in the 12-week change in visual acuity. The a priori critical threshold for the superiority hypotheses is 0, and the a priori critical threshold for the non-inferiority related hypotheses is 0.10. The *P* value for each null hypothesis test is provided in parenthesis, and any one-sided confidence interval in A or B that crosses the critical threshold and extends to the right of the critical threshold indicates that the null hypothesis fails to be rejected at the .05 significance level. Intervention denotes the video game group, whereas control refers to the eye patching group.

DISCUSSION

Consistent with our research hypothesis, the video game treatment showed statistical non-inferiority to eye patching as a home-based treatment for nonstrabismic amblyopia after 12 weeks of treatment. Both our cross-sectional and longitudinal analyses showed similar improvements in visual acuity of approximately 0.14 logMAR in both groups after 12 weeks of respective treatments. The results appear to be clinically relevant and in line with previous studies that showed greater BCVA improvements in participants with amblyopia and higher time efficiency compared to patching following longer durations of video game treatment regimens.[15]

In the Barron Vision video games, practiced at various levels of stimulus difficulty and task challenge over a 12-week period, discrimination of red target optotypes is based not only on their size, but also retinal location, orientation, and motion direction. All of these attributes are important for perceptual learning, which has recently found resurgence in studies evaluating its applicability to treatment of amblyopia in pediatric, adolescent, and adult samples. The classic definition of perceptual learning by Gibson[16] refers to "any relatively permanent and consistent change in the perception of a stimulus array, following practice or experience with this array." With the development of interactive software tools, several studies found significant improvements in visual performance, visual acuity, and contrast sensitivity in patients with amblyopia of various ages after repeated training with various perceptual learning tasks under monocular occlusion conditions of the sound eye.[17-20] It is hypothesized that perceptual learning can lead to permanent changes in both performance and neural processing at an early stage of visual coding at the level of the primary visual cortex through stimulation of neuroplasticity.[21] Indeed, Polat et al[19] examined changes in visual acuity at 3, 6, 9, and 12 months following perceptual learning training in individuals with amblyopia and found only a small decrement in acuity. Similarly, Zhou et al[22] reported that visual acuity level was almost fully preserved after as much as 18 months follow-

ing cessation of perceptual learning training. Thus, the improvement in acuity resulting from perceptual learning seems to be long-lasting and equally beneficial for pediatric, adolescent, and even adult patient cohorts.

Furthermore, it has been suggested that perceptual learning improves performance via higher order attentional modulation.[21] For example, it has been reported that games requiring precise rapid visual analysis to guide accurate aiming movements appear to be the most efficient in improving visual attention.[15] This attentional enhancement may be directly relevant to treatment of amblyopia, because one of the proposed etiological mechanisms of amblyopia is suppression of one eye by signals from higher attentional brain regions.[15] In the current study, rapid temporal processing of the visual stimuli within the games, including aiming at targets, monitoring of the periphery that required quick and accurate motor actions, multiple object tracking, and rapid target identification in an array of distractors, may all have contributed to improved visual acuity in the amblyopic eye due to improved temporal processing the amblyopic eye, the fellow eye, and the amblyopic brain.

When it comes to patching, the regimen used in the control group in the current study was based on the procedures employed in the randomized trial of treatment of amblyopia in children aged 7 to 17 years by the Pediatric Eye Disease Investigator group.[6] In their study, a patient was considered a responder if the amblyopic eye visual acuity was two lines or better than the baseline acuity on the ETDRS chart (≥ 0.2 logMAR) at the end of the 24-week treatment period. In that study, analyses were conducted separately for the 7 to 12 and 13 to 17 year age groups. This was due to the application of atropine drops (1% atropine sulphate) to the non-amblyopic eye in the younger age group in addition to the prescribed patch treatment and near work activities. Atropine drops were administered once daily when the non-amblyopic eye was not patched. The application of atropine was not used in the older age group to prevent interference with daily activities requiring sustained attention such as driving. Consequently, the percentage of responders was 53% in the younger age group but only 25% in the older group. The researchers hypothesized that a synergistic effect of patching combined with atropine administration was driving more marked improvements in the 7 to 12 year olds. The researchers had no way of separating the effect of patching in this group from atropine administration. In the current study, participants in the eye patching group did show significant improvements in their amblyopic eye at the end of the 12-week treatment period, with a mean improvement of -0.131 logMAR. Nonetheless, the results of the study also showed non-inferiority of the Barron Vision video game therapy that produced similar increments in acuity (-0.122 logMAR) after 12 weeks.

The latter results are encouraging because the video game treatment consisted of only 20 minutes of play 5 days a week, irrespective of baseline visual acuity in the amblyopic eye. This was in stark contrast with at least 120 minutes of daily patching in the 20/200 or better visual acuity group and 360 minutes in the group with visual acuity worse than 20/200. Although effective, this stringent patching regimen has been previously reported to be fraught with compliance issues.[3,8] Similarly, in the pediatric amblyopia study,[2] compliance could not be adequately assessed because only half of the original sample returned their self-report log forms tracking treatment compliance. In the current study, although the difference between the eye patching and video game groups in percent compliance with the prescribed treatment was not statistically significant, participants in the video game group showed a trend toward better compliance (85.7% compared to 79.5%). It should also be noted that in our study compliance was reinforced by weekly calls from each site's therapist and a requirement to bring home log forms to each follow-up visit. In clinical practice, home-based eye patching is not rigorously monitored or enforced.

Study Limitations

A significant limitation of this study was the coronavirus disease 2019 (COVID-19) pandemic, which had an adverse impact on study site staffing and on participant recruitment and retention. Pandemic-related concerns (including regional restrictions, temporary closure of certain clinics, loss of staff, and general fear) were largely responsible for the observed attrition rate of 22.5%. Limitations also include a potential for selection bias, due to volunteers being more motivated to comply with the proposed treatment regimen than the average patient. Additionally, the study did not include any

follow-up periods after cessation of the treatment to monitor for risk of amblyopia recurrence or loss of treatment effectiveness.

CONCLUSION

This randomized controlled trial contributes to the existing body of knowledge by providing evidence that a 12-week home-based video game vision therapy intervention (Barron Vision) can provide equivalent treatment outcomes to eye patching for amblyopia in children ages 5 to 18 years. Video game–based vision therapy may be a more acceptable and time-efficient alternative to existing approaches. By incorporating elements of perceptual learning, approaches such as the Barron Vision system may have additional long-term therapeutic benefits.[15] This hypothesis needs to be further evaluated in larger pediatric samples with longer follow-up periods.

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