Review

Binocular Approaches in Amblyopia Treatment Based on Dichoptic Stimulation

Demet Yabanoğlu, Hande Taylan Şekeroğlu

Hacettepe University Faculty of Medicine, Department of Ophthalmology, Ankara, Türkiye

Abstract

The discovery that binocular dysfunction may play a critical role in the development of amblyopia has led to the development of a novel approach based on contrast-rebalanced binocular stimulation of both eyes. This approach, known as dichoptic stimulation, enables the treatment of amblyopia by facilitating the cooperation of both eyes. Dichoptic treatment approaches are founded on the theoretical premise that binocular imbalance plays a significant role in both monocular and binocular impairments in amblyopia, and that preserving binocular function capacity is essential. Therefore, these approaches are designed to promote the collaborative functioning of the eyes, enhance stereopsis, and improve binocular fusion. This review systematically examines and synthesizes the existing literature on dichoptic stimulation techniques aimed at improving binocular function in the treatment of amblyopia. Based on various studies in the literature, the fundamental principles of these treatment methods are outlined, and the results obtained in comparison to traditional monocular treatments are highlighted. The clinical efficacy of dichoptic treatment methods is evaluated in terms of their contribution to enhancing binocular function in amblyopia. Additionally, information is provided regarding the outcomes, treatment durations, efficacy levels, and potential side effects of these treatment approaches in different patient groups. This review offers a comprehensive assessment of the integration of dichoptic treatment approaches into clinical practice, highlighting both their advantages and disadvantages, and aims to provide a guiding perspective on their future use.

Cite this article as: Yabanoğlu D, Taylan Şekeroğlu H. Binocular Approaches in Amblyopia Treatment Based on Dichoptic Stimulation. Turk J Ophthalmol. 2025;55:148-158

Address for Correspondence: Demet Yabanoğlu, Hacettepe University Faculty of Medicine, Department of Ophthalmology, Ankara, Türkiye
E-mail: demet.aban@hacettepe.edu.tr **ORCID-ID:** orcid.org/0000-0003-4532-3543
Received: 14.08.2024 **Accepted:** 07.01.2025

DOI: 10.4274/tjo.galenos.2025.06626

Keywords: Amblyopia, binocular dysfunction, binocular therapies of amblyopia, dichoptic stimulation

Introduction

Binocular Dysfunction and Amblyopia

Amblyopia is defined as a visual impairment caused by abnormal binocular interaction and disproportionate fusional suppression in one or both eyes during early visual development with no underlying abnormality or pathology detected with routine eye examination.[1,2,3] Although amblyopia can occur in both eyes, it was historically considered a monocular condition because visual acuity is typically affected in only one eye. Consequently, traditional amblyopia treatments aimed to improve the monocular visual acuity of the amblyopic eye by suppressing the other (dominant) eye, which was thought to be healthy.[4-23] While these treatments could be effective in enhancing the visual acuity of the amblyopic eye, they did not prevent the occurrence of residual or recurrent amblyopia, ocular motor problems, fine motor issues, and contrast sensitivity abnormalities in many individuals.[24,25]

The discovery that binocular vision is necessary for the amelioration of experimentally induced amblyopia in animal models led to the hypothesis that binocular dysfunction plays a critical role in the development of amblyopia.[26] Subsequent findings that balanced contrast in the two eyes can lead to binocular vision were regarded as evidence of latent binocular abilities in amblyopic individuals.[27,28] Given that binocular dysfunction is thought to be an important factor in the development of amblyopia, many researchers suggest that binocular approaches may play a significant role in the treatment of amblyopia.[3,24,29] This perspective has led to the development of a new dichoptic stimulation approach that relies on binocular stimulation conditions forcing both eyes to collaborate on a visual task by balancing the contrast differences between them.[29]

Dichoptic stimulation involves presenting different images to each eye and posing a visual task that can only be completed by combining information from both eyes.[24] These stimuli can be provided using red/green anaglyph glasses (glasses with one red and one green lens, used to view stereoscopic pictures/video consisting of two images of the same object/scene taken from slightly different angles), shutter glasses (glasses that brighten and darken quickly in sync with the monitor, thus allowing a common background to be presented to both eyes but allowing the rich, moving image to be presented only to the amblyopic eye), polarized glasses, virtual reality (VR) headsets, or low-pass filters that reduce brightness in the dominant eye.

Dichoptic contrast stimulation involves presenting different images with varying contrast levels to each eye, while maintaining the same background contrast for both eyes. The dichoptic manipulation of contrast is achieved by reducing the contrast of the signal seen by the dominant eye to a point where binocular combination is possible, thus eliminating suppression from the dominant eye. This delicate balance point can vary for each amblyopic individual. It is thought that allowing the eyes to combine information under balanced contrast conditions and repeatedly exposing the amblyopic individual to these stimuli will progressively strengthen binocular fusion, eventually resulting in smaller interocular contrast differences.[24,27,28]

Dichoptic approaches are based on the assumption that the amblyopic visual system retains its binocular functional capacity (latent binocular abilities).[3,24] The primary objective of dichoptic approaches is to restore binocular fusion and stereopsis, with the expected secondary outcome of improved visual acuity in the amblyopic eye.[3] To achieve this, complementary dichoptic stimuli are employed, such that the visual task can only be resolved if both left and right eye information is integrated.[24]

The purpose of the present review is to evaluate dichoptic stimulation approaches for the treatment of amblyopia in light of published studies on the subject. Binocular approaches are examined in three sections: the first section covers dichoptic stimulation approaches designed to restore monocular visual acuity; in the second section we discuss monocular perceptual learning and dichoptic stimulation approaches aimed at restoring binocular function; and the third section addresses active and passive dichoptic stimulation approaches and dichoptic contrast manipulation designed to restore binocular function.

1. Approaches Using Dichoptic Stimulation to Improve Monocular Visual Acuity

The aim of these approaches is to develop an amblyopia treatment alternative to patching therapy, enhancing visual acuity in a fun, binocular format for children.[30]

Interocular Binocular Treatment System

Interocular binocular treatment system (I-BiT™) is a VR-based computer system that uses dynamic stimuli for preferential stimulation of the amblyopic eye without the need for patching. The original I-BiT™ system features a 3D cyberscope,[30] which allows rapid light and dark alternation synchronized with the monitor, presenting a common background to both eyes while a rich, dynamic image is delivered only to the amblyopic eye. In this setup, two completely separate but visually related images can be presented independently to each eye, similar to a synoptophore.[31,32] In this system, images are presented to the eyes with various methods.[30] These methods have been used to develop different video clips and games. In the video clips, the amblyopic eye sees a moving video, while the dominant eye sees a stationary background. The games used in the I-BiT™ system include a version of Pac-Man (Bandai Namco Entertainment Inc., Japan) and a racing game. Studies implementing I-BiT™ are summarized in Table 1.[33,34,35,36]

The I-BiT™ system was tested in a pilot study involving 6 children aged 5-7 years with anisometropic, strabismic, or combined anisometropic/strabismic amblyopia in which traditional treatments were refused or failed.[33] The study involved 1-2 treatment sessions per week, with each session including 20 minutes of video viewing and a few minutes of interactive gameplay. Treatment continued until the visual acuity of the amblyopic children stabilized (11-22 months), showing a mean improvement of 10 letters in logarithm of the minimum angle of resolution (logMAR) visual acuity.[33]

In a multicenter, randomized controlled trial involving 75 patients aged 4-8 with strabismic, anisometropic, or mixed amblyopia, the I-BiT™ system produced a visual acuity improvement of 0.067 logMAR after 10 weeks.[32] However, no gains were observed in stereoacuity. It was concluded that dichoptic stimulation with I-BiT™ did not provide a significant advantage for the amblyopic eye. The limited success in the study was attributed to the short treatment duration, a high rate of previous treatment failures among the participants, and the disadvantage of strabismic amblyopia in dichoptic stimulation studies.[34]

I-BiT™ is considered an effective supplementary method for amblyopia treatment, but no sustained improvement in visual acuity was observed after it was discontinued.[35] Issues with adherence in the I-BiT™ system have been pointed out, mainly due to the prototype's unsuitability for young children and inability to be used at home.[32,34] Researchers also emphasized the need for dichoptic images to be presented in alignment with each eye's fovea for success in strabismic and mixed amblyopia cases.[31]

2. Approaches Using Monocular Perceptual Learning and Dichoptic Stimulation to Restore Binocular Function

Research has shown that performing a challenging visual task repeatedly can enhance perceptual performance, particularly in adults and older children in whom traditional treatments have limited success in improving visual acuity.[22,23] However, the limited improvement in visual acuity and the restriction of perceptual learning due to monocular occlusion as a routine treatment for amblyopia have been noted. To overcome these limitations, researchers have developed alternatives with the aim of providing perceptual learning under binocular conditions.

Table 1. Studies implementing I-BiT™ to improve monocular visual acuity

Studies	Study type	Sample size	Amblyopia type	Age	Treatment duration	Session duration/ frequency	Adherence	Stereoacuity improvement	Visual acuity improvement	Side effects
Waddingham et al.[33] 2006	Pilot	6	Anisometropic, strabismic, or mixed	5-7	11-22 months	20 min, 2 days/week	100%	N/A	10 letters	None
Herbison et al.[32] 2013	Pilot	10	Anisometropic, strabismic, or mixed	4-8	6 weeks	30 min, 1 day/week	90%	N/A	0.18 logMAR	None
Herbison et al.[34] 2016	Randomized controlled	75	Anisometropic, strabismic, or mixed	4-8	6 weeks	30 min, 1 day/week	>90%	None	0.060 logMAR	Diplopia
Rajavi et al.[35] 2016	Randomized controlled	50	Anisometropic	3-10	4 weeks	30 min, 5 days/week	N/A	N/A	0.17 logMAR	N/A
Rajavi et al.[36] 2019	Randomized controlled	38	Anisometropic	3-10	4 weeks	30 min, 5 days/week	87.5%	None	0.08 logMAR	N/A

I-BiT™: Interocular binocular treatment system, N/A: Not applicable (not assessed or reported in study), logMAR: Logarithm of the minimum angle of resolution

Push-Pull Perceptual Learning Training Protocol

The visual sensory system can be shaped by competition from binocular stimulus interactions and reciprocal inhibition between the two eyes.[37] In normally developed adults, reciprocal inhibition between the eyes is generally balanced. However, disruption of this balance results in sensory eye dominance.[37] It is thought that almost all individuals exhibit some degree of sensory eye dominance.[38] When this dominance becomes excessive, it leads to disturbances in binocular vision through both excitatory and inhibitory mechanisms.[37] Amblyopia is described as a condition in which excessive interocular inhibition of the amblyopic eye occurs as a result of extreme sensory eye dominance.[39]

It has been reported that amblyopic individuals exhibit more pronounced sensory eye dominance compared to healthy controls with clinically normal visual acuity.[40] Push-pull perceptual learning training (PPLT) was developed as a protocol to reduce excessive sensory eye dominance in amblyopia and improve stereopsis by simultaneously affecting the excitatory stimuli of the amblyopic eye and the inhibitory stimuli of the dominant eye.[37] Traditional amblyopia treatments, such as occluding the dominant eye, do not directly address sensory eye dominance.[37] PPLT is fundamentally designed to regulate the binocular balance of excitatory and inhibitory interactions by suppressing the dominant eye's perception (pull) and stimulating the amblyopic eye's perception (push). It has been noted that this training protocol effectively reduces sensory eye dominance, improves stereoacuity, and significantly contributes to sensory plasticity even in people with clinically normal binocular vision.[37,38,39,40] This method has been proposed as a potentially effective treatment for amblyopia. However, the only clinical study on PPLT conducted so far involved 36 children aged 4-17 with anisometropic amblyopia and 33 with normal visual acuity. The 20-minute training sessions stimulated both the visual cortex and the temporal lobe, highlighting the importance of this method for regaining stereoacuity in anisometropic amblyopia.[41] The persistence of learning effects for more than 4 months after training suggests that PPLT induces long-term cortical plasticity.[38]

Lazy Eye Shooter

Lazy Eye Shooter is a therapeutic video game created by modifying the first-person action game Unreal Tournament 2004 (Epic Games, 2004, CA, USA). In this method, the amblyopic individual views the same game scene on two different screens using a stereoscope or video glasses (Figure 1). This approach simultaneously provides perceptual learning, video gameplay, and dichoptic stimulation. Amblyopic individuals are asked to play a specially designed action video game with monocular perceptual learning tasks, Gabor patches,[42] and dichoptic stimulation. Gabor patches are sinusoidal gratings featuring a pattern of diagonal black and white stripes enclosed within a square frame.[43] They are commonly used in studies of amblyopia, particularly in the context of perceptual learning. In the dichoptic presentation method developed by Bayliss et al.[43], the same image (except for the Gabor patches) is shown to each eye with reduced contrast for the dominant eye, with the aim of encouraging binocular fusion. As part of the game, participants are required to shoot at targets containing a Gabor patch while ignoring those without it.[43]

In a study comparing Lazy Eye Shooter with occlusion therapy in 38 adults aged 19-66, the game group showed a significant improvement in visual acuity (0.14±0.01 logMAR) after 40 hours of treatment.[44] Significant improvements were also observed in stereoacuity, with a mean gain of 0.18±0.05 log seconds of arc (arcsec). Additionally, participants who received dichoptic and perceptual learning training showed markedly enhanced contrast ssensitivity and reading speed and reduced fear of losing vision in the dominant eye, with these improvements remaining stable even after 2 months.

However, this therapeutic approach has some limitations. Due to the inclusion of violent elements (weapons, blood, and violence), Lazy Eye Shooter cannot be used for children.[44] The

Figure 1. Lazy Eye Shooter game. Two game screens are shown. The good eye is shown the dimmed screen (right) and the amblyopic eye is shown the screen with the extra object (Gabor patch; left) (Reproduced from Bayliss JD, Vedamurthy I, Bavelier D, Nahum M, and Levi D, "Lazy eye shooter: A novel game therapy for visual recovery in adult amblyopia", *2012 IEEE International Games Innovation Conference*, Rochester, NY, USA, 2012, pp. 1-4, with permission from *IEEE Proceedings*)

requirement to play the game for approximately 40-50 hours can also lead to boredom among participants. Additionally, the Gabor patches as currently designed interrupt the flow of the game and affect the player's concentration.[43,44]

3. Approaches Using Dichoptic Stimulation with Contrast Manipulation to Restore Binocular Function

Interactive Approaches

Falling Blocks

Falling Blocks is a modified version of the game Tetris (Tetris Inc., Honolulu, HI, USA). Tetris was chosen for dichoptic stimulation due to its block-based structure, which enables effective contrast customization.[45] In the initial prototype developed, the contrast balance ratio was calculated individually for each person to determine how blocks should be presented to the amblyopic and dominant eyes. The amblyopic individual advances to higher levels by creating rows of blocks without gaps. At higher levels, the difficulty of the game is raised by recalculating the contrast balance ratio and increasing the block fall speed, while maintaining an effect that does not significantly impact game performance.[45]

The dichoptic stimulation in this game can be presented in various ways. Knox et al.[46] performed this application using VR glasses in an office setting, while To et al.[45] used a touch-sensitive iPod® Touch (Apple® Inc., Cupertino, CA, USA) without requiring additional equipment in an office setting. However, due to the need for a fixed head position and excellent fine motor skills for manipulating the blocks, this design was not suitable for younger amblyopic children.[47] Consequently, the game was modified to be played on a larger iPad® (Apple® Inc., Cupertino, CA, USA) held at reading distance while wearing red/green anaglyph glasses.[47,48,49,50,51] Game elements are presented with 100% contrast to the amblyopic eye and lower contrast to the other eye. The contrast used for the dominant eye is adjusted based on the game duration and previous day's performance, with changes ranging from an increase of 10% to a reduction or no change. Studies implementing Falling Blocks are summarized in Table 2.[47,48,50,51,52,53,54,55,56]

Two multicenter randomized clinical trials conducted by the Pediatric Eye Disease Investigator Group (PEDIG) compared the effects of Falling Blocks therapy and occlusion therapy on amblyopic eye visual acuity.[50,51] These studies involved 385 children aged 5-12 and 100 adolescents aged 13-16 with strabismic (≤4 prism diopters [PD]), anisometropic, or mixed-type amblyopia. In the trials, a 16-week home-based treatment of 1 hour per day with the binocular Falling Blocks game was compared to 2 hours per day of recommended occlusion therapy. The touch device recorded game play duration and dominant eye contrast automatically. Over the 16-week period, the binocular treatment group completed at least 75% of the prescribed treatment 22% of the time in the 5-12 age group and 13% of the time in the 13-16 age group. Improvements were observed in amblyopic eye visual acuity, with a mean gain of 1.05 lines (0.31 lines difference favoring occlusion) in the 5-12 age group and 0.74 lines (0.52 lines difference favoring occlusion) in the 13-16 age group. However, no significant changes in stereoacuity measurements were reported in the binocular treatment groups compared to baseline values.[50,51]

Overall, studies involving Falling Blocks therapy suggest that this treatment may provide more significant improvements in visual acuity and stereoacuity in amblyopic adults.[45,47,48,49,50,51] Differences in study outcomes may be attributed to whether the contrast balance points were individualized, age-related differences in attention or motivation, and variations between controlled laboratory and home settings.[48] PEDIG has suggested that visual acuity improvements with Falling Blocks therapy are not as effective as 2 hours per day of occlusion therapy.[50,51] Possible reasons for these results include the timing of initial and final evaluations and differences in treatment duration. In some studies, patients were assessed after shorter treatment periods (4 weeks),[45,47,48] while in the PEDIG trials they were evaluated after

Table 2. Studies implementing active dichoptic stimulation and dichoptic contrast manipulation designed to regain binocular function

Studies	Study type	Sample size	Amblyopia type	Age	Treatment duration	Session duration/ frequency	Adherence	Stereoacuity improvement (mean, log arcsec)	Visual acuity improvement	Side effects
Falling Blocks										
Li et al.[48] 2014	Case-control	75	Anisometropic, strabismic, or mixed	4-12	4 weeks	4 hours/week	N/A	11%	0.08±0.01 logMAR	N/A
Birch et al.[47] 2015	Case-control	50	Anisometropic, strabismic, or mixed	3-7	4 weeks	4 hours/week	59%	None	0.14±0.02 logMAR	N/A
Holmes et al.[50] 2016	Randomized controlled	385	Anisometropic, strabismic, or mixed	5-12	16 weeks	1 hour/week	22%	None	1.05 lines	Heterotropia, diplopia
Manh et al.[51] 2018	Randomized controlled	100	Anisometropic, strabismic, or mixed	13-16	16 weeks	1 hour/week	13%	None	3.7 letters or 0.74 lines	Heterotropia, diplopia
Dig Rush										
Kelly et al.[52] 2016	Randomized controlled	28	Anisometropic, strabismic, or mixed	4-10	2 weeks	5 days/week, 1 hour/day	100%	None	0.15±0.08 logMAR	None
Kelly et al.[54] 2018	Randomized controlled	41	Anisometropic, strabismic, or mixed	4-10	2 weeks	5 days/week, 1 hour/day	94%	4.46±0.79	0.14±0.09 logMAR	N/A
Holmes et al.[55] 2019	Randomized controlled	138	Anisometropic, strabismic, or mixed	7-12	8 weeks	5 days/week, 1 hour/day	97%	None	2.3 letters	Heterotropia, diplopia
Manny et al.[56] 2022	Randomized controlled	182	Anisometropic, strabismic, or mixed	4-6	8 weeks	5 days/week, 1 hour/day	78%	None	1.3 logMAR	Diplopia

N/A: Not applicable (not assessed or reported in study), logMAR: Logarithm of the minimum angle of resolution, arcsec: Seconds of arc

a longer period (16 weeks).[50,51] However, Li et al.[49] proposed that visual acuity improvements from binocular treatment can persist for up to 12 months. Another reason for the lack of a larger effect may be that participants lost interest in the game, highlighting the importance of addressing compliance issues and developing more engaging treatment alternatives such as immersive children's games, binocular first-person action games, and binocular film watching.

Dig Rush

Dig Rush is an action-adventure game played on an iPad using red/green anaglyph glasses. Detailed information about the game is presented by Kelly et al.[52] The red/green anaglyph glasses enable the presentation of distinct game elements to each eye. In the game, high-contrast elements (miners and monsters) can be seen by the amblyopic eye, while the low-contrast elements (mining cart, gold, and fire) can be seen by the dominant eye (Figure 2).[53] The game starts with the amblyopic eye's contrast set to 100%, while the contrast level of the dominant eye can be adjusted by the clinician. Success in the game leads to an increase in the dominant eye's contrast, while a lack of success over 30 minutes results in a reduction in contrast. The touch device automatically records gameplay duration and dominant

Figure 2. Dig Rush. High-contrast red elements (miners and fireball) are seen by the amblyopic eye. Low-contrast blue elements (gold and platforms) are seen by the dominant eye. Gray elements (rocks and ground) are seen by both eyes (Reproduced from Boniquet-Sanchez and Sabater-Cruz[53] with permission from *Vision*)

eye contrast, adjusting the contrast based on the success rate.

Studies concerning Dig Rush are summarized in Table 2. In two multicenter randomized controlled trials, PEDIG compared the effects of Dig Rush on amblyopic eye visual acuity with those of using glasses alone.[55,56] The first of these studies included 138 children aged 7-12 with strabismic (≤4 PD), anisometropic, or mixed amblyopia, and objective adherence to the therapy was 58% at 4 weeks and 56% at 8 weeks. The binocular treatment group showed an improvement in amblyopic eye visual acuity of 1.3 letters at 4 weeks and 2.3 letters at 8 weeks. However, no significant differences were observed in stereoacuity measurements compared to baseline values.[55]

The age groups included in Dig Rush studies vary. Kelly et al.[52,54] included children aged 4-10, while the PEDIG studies[55,56] involved children aged 7-12 and 4-6. Differences in results among these studies have been attributed to the varying age groups.[54,55] Older age groups may have a history of previous amblyopia treatments (e.g., occlusion and atropine) or may have reached a treatment plateau with limited additional improvement from new therapies, making them less responsive to binocular treatments. Younger age groups and/or children who have not undergone amblyopia treatment previously might be more responsive to binocular treatments. However, when the same protocol was applied to children aged 4-6, visual acuity improvements observed at 4 weeks were not maintained at 8 weeks. Variability in adherence to the prescribed treatment duration has also been suggested as a reason for inconsistent results.[54,55] In the studies by Kelly et al.,[52,54] higher adherence rates (87-100%) were linked to significant improvements in visual acuity and binocular outcomes. In contrast, the PEDIG study found adherence rates of 56-75% among children aged 7-12 years.[55] PEDIG attributed this to the design of the Dig Rush game, which was assumed to be more appealing to younger children, and therefore anticipated higher adherence in a subsequent study involving children aged 4-6 years. However, contrary to expectations, lower adherence rates of 43-57% were observed in this younger age group.[56] These findings suggest that adherence to the Dig Rush game may vary depending on age group and individual characteristics, highlighting the importance of accounting for age-related differences when evaluating the effectiveness of game-based therapies.

Vivid Vision®

Vivid Vision® (Vivid Vision Inc., San Francisco, CA, USA) games provide a dichoptic visual experience using VR glasses. Originally named Diplopia, the games are now known by the company's name, Vivid Vision®. In Diplopia mode, designed in 2014 by Blaha (who himself suffered from strabismus and amblyopia) and Gupta[57], each eye receives a different image, compelling the eyes to work together to succeed in the game. The aim is to limit the information given to each eye, requiring the player to integrate both visual inputs into a single coherent image.

In a pilot study involving 17 adults aged 17-69 with anisometropic amblyopia, after 4 weeks of Vivid Vision® games played in twice-weekly sessions lasting 40 minutes, there were significant improvements in both visual acuity and stereoacuity in the amblyopic eye (Figure 3).[58] These improvements were correlated with in-game test measurements, and no persistent diplopia or other adverse effects were reported.[59]

However, Vivid Vision® games have limitations. Developers note that simulator sickness[60] caused by VR glasses poses a significant barrier, especially for children. Additionally, the VR glasses' inability to monitor changes in accommodation and the design not fitting well around the head are other reasons why the system cannot be used for younger children. There is also concern about the risk of abnormal retinal correspondence developing in strabismic amblyopia cases.

Passive Approaches

Contrast-Balanced Dichoptic Movies

Dichoptic films consist of long-format versions of popular animated films or television programs presented in a dichoptic format. These films can be viewed using polarized[61,62,63] or shutter glasses,[64] VR headsets,[65] or specialized devices[66] without additional imaging equipment. An example of such a film is shown in Figure 4.

In a pilot study involving 8 patients aged 4-10 years with strabismic (≤5 PD), anisometropic, or mixed amblyopia, the impact of watching dichoptic films in a laboratory setting for 2 weeks, 3 times a week was evaluated in terms of visual acuity, stereoacuity, and interocular suppression.[61] A significant improvement in mean visual acuity of 2.0 logMAR was reported in the amblyopic eye. No significant changes were observed in stereoacuity or interocular suppression. This level of improvement was notably greater in the younger age group (3-6 years) and in cases of severe amblyopia (≥0.7 logMAR).[62] In cases of anisometropic amblyopia with measurable stereoacuity values (170 arcsec) at the start of treatment, there was a significant increase in stereoacuity (85 arcsec) following treatment.[64] Additionally, this gain in stereoacuity was significantly related to both the initial visual acuity of the amblyopic eye and the absolute improvement in visual acuity. Studies in which passive dichoptic approaches were implemented are summarized in Table 3.

In a study involving 17 amblyopic individuals with a mean age of 34 years, it was demonstrated that patching the amblyopic eye for 2 hours prior to therapeutic film sessions resulted in significant visual acuity improvement in the amblyopic eye, with sustained gains observed during a 1-month follow-up.[63] That study indicated that short-term monocular deprivation might activate binocular brain plasticity mechanisms through changes in excitatory/inhibitory balance, potentially enhancing dichoptic training outcomes.[63]

These findings constitute preliminary evidence that passive dichoptic film training can improve stereoacuity in older children and amblyopic adults. Furthermore, a 2-week treatment period with films viewed 3 times a week was found to be more effective in enhancing visual acuity and stereoacuity than patching for 2 hours daily.[66]

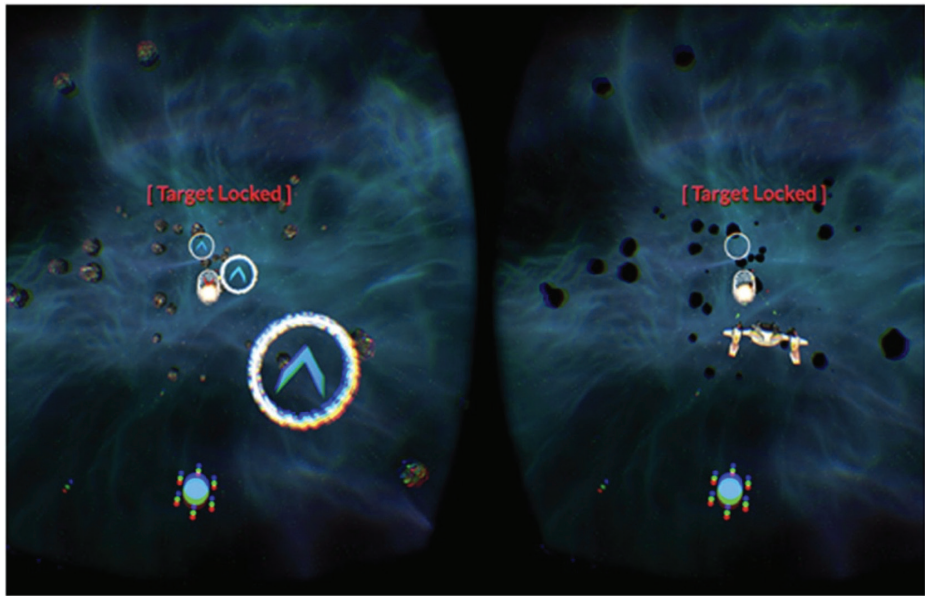

Figure 3. Vivid Vision® Ring Runner. This space game is designed with a dichoptic environment in which the central part of the image is different. Colored doors and asteroids can only be seen with the amblyopic eye, while the spaceship can only be seen with the dominant eye. The spaceship is presented to the dominant eye to prevent cheating, because if all objects in the game are seen with the amblyopic eye, there is a risk that the patient can monocularly use the amblyopic eye by closing the dominant eye (Reproduced from Žiak et al.[58] with permission from *BMC Ophthalmology*)

The most recent development in dichoptic films is Luminopia™ One (Luminopia Inc., Cambridge, MA, USA) digital therapy. As the first FDA-approved digital therapy, Luminopia™ One allows children aged 4-7 with anisometropia and/or mild strabismus, under the supervision of an ophthalmologist, to watch approximately 700 hours of popular television programs and films through a VR headset.[67] Given the issues associated with VR headset use in younger children, Luminopia™ One has been specifically designed with adjustable interpupillary distance and a secure strap system to accommodate children's heads. The device's therapeutic visual input, delivered to each eye via the VR headset, is controlled by a software application preloaded onto a smartphone.

Following encouraging results from a pilot study,[68] a multicenter randomized controlled trial was conducted to compare full-time refractive correction to 12 weeks of dichoptic therapy using Luminopia™ One for 1 hour per day, 6 days per week.[65] The results of the trial demonstrated that after 12 weeks of treatment, amblyopic eye visual acuity was significantly better in the dichoptic treatment group compared to the full-time refractive correction group.

Controversial Aspects of Dichoptic Stimulation-Based Binocular Approaches

Research involving binocular approaches using dichoptic stimulation has increased interest in the development of amblyopia treatments that directly address binocular dysfunction by promoting binocular vision and reducing inhibitory interactions within the visual cortex.[3,24] Although improvements in stereoacuity have been reported in pilot studies,[39,41,43,47,58,64] these

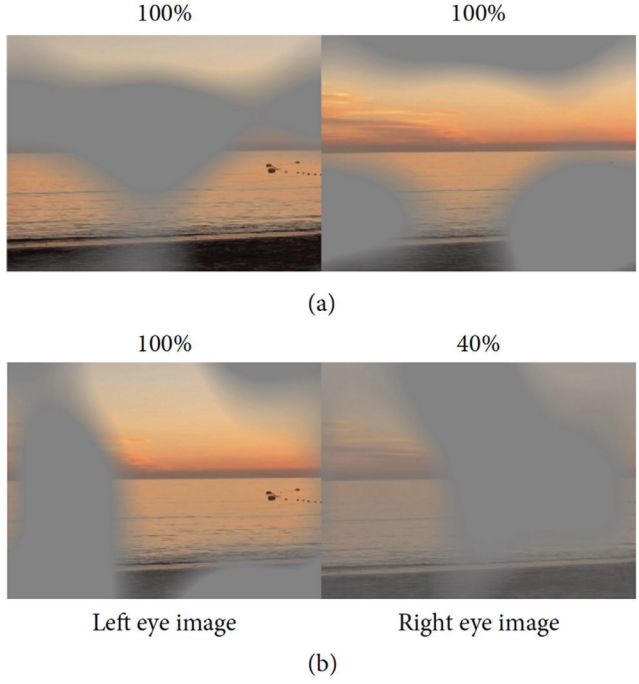

Figure 4. Dichoptic film sections (a, b) at 10-second intervals. a) 100% contrast of the images are presented to both eyes. b) High contrast image is presented to the amblyopic eye, while low contrast image is presented to the dominant eye. (Reproduced from Sauvan et al.[63] with permission from *Neural Plasticity*)

Table 3. Studies implementing passive dichoptic stimulation and dichoptic contrast manipulation designed to regain binocular function

Studies	Study type	Sample size	Amblyopia type	Age (y)	Treatment duration	Session duration/ frequency	Adherence	Stereo acuity improvement	Visual acuity improvement	Side effects
Dichoptic movies										
Li et al.[61] 2015	Prospective cohort	8	Anisometropic, strabismic, or mixed	4-10	2 weeks	3 days/week	N/A	None	2 logMAR	N/A
Birch et al.[62] 2019	Prospective cohort	27	Anisometropic, strabismic, or mixed	4-10	2 weeks	3 days/week	N/A	None	0.15±0.10 logMAR	N/A
Sauvan et al.[63] 2019	Prospective cohort	17	Anisometropic, strabismic, or mixed	9-67	2 weeks	3 days/week	N/A	N/A	0.08 logMAR	N/A
Jost et al.[66] 2022	Randomized controlled	60	Anisometropic, strabismic, or mixed	3-7	2 weeks	3 days/week	95%	0.12 log arcsec	0.07 logMAR	N/A
Bossi et al.[64] 2017	Cohort	22	Anisometropic, strabismic, or mixed	3-11	8 weeks	1 hour/day	68%	165±182 log arcsec	0.39±0.25 logMAR	None
Luminopia™ One										
Xiao et al. 2022[65]	Randomized controlled	105	Anisometropic, strabismic, or mixed	4-8	12 weeks	1 hour/day, 6 days/week	88.2%	None	0.18 logMAR	Headache, heterotropia

N/A: Not applicable (not assessed or reported in study), logMAR: Logarithm of the minimum angle of resolution, arcsec: Seconds of arc

results have not been corroborated by multicenter randomized controlled trials. Key uncertainties remain regarding the optimal reduction in contrast in the dominant eye, the rate of contrast progression throughout treatment, and whether therapy should continue once equal contrast is achieved.[50,51] The variability in amblyopia severity among individuals underscores the necessity for personalized determination of initial and ongoing contrast ratios for each amblyopic patient.[45] Additionally, the lack of a stereoacuity test that measures thresholds between 0 and 2000 arcsec has led to a decrease in the number of individuals with measurable stereoacuity at baseline, and the use of different stereoacuity tests across heterogeneous age groups may lead to non-comparable results.[46] Furthermore, there is concern about whether the improvements observed with binocular therapy are due to learning effects. However, studies evaluating the visual acuity of the dominant eye no significant increases, suggesting that improvements in the amblyopic eye are not likely to be a result of learning.[50,51,55,56,61,62,63,64]

To effectively deliver dichoptic-based binocular therapy, reach the maximum number of patients, and compete with monocular approaches, there is a pressing need for home-based treatment alternatives.[45] However, the most effective models in vision therapy are typically office-based, doctor-supervised, and tailored to individual patient goals. Moreover, inconsistencies between electronic records of adherence to binocular therapy and parent-reported adherence, uncertainties about actual use of the required equipment, and the possibility that the therapy may not be administered by the amblyopic patient themselves raise questions about the reliability of home-based treatments.[50,51,55,56]

In studies on binocular therapy involving participants with strabismic or mixed-type amblyopia, only those with a deviation angle of 4-5 PD or less following surgery or glasses were included. Researchers have emphasized that results should not be generalized to other forms of amblyopia, such as those with a greater deviation angle or deprivation amblyopia (e.g., congenital cataracts).[52,54]

Since the mechanism of action of dichoptic stimulation-based binocular treatments may involve anti-suppression pathways, concerns have been raised that these therapies could be associated with new-onset diplopia. However, diplopia has been rarely reported in these studies.[50,56]

Although interest in binocular approaches for amblyopia rehabilitation grows, the number of studies investigating the effect of dichoptic stimulation on the crowding phenomenon remains quite limited.[69,70] It is known that contrast sensitivity loss in amblyopia increases the crowding effect under monocular conditions. In perceptual learning-based amblyopia treatments, it has been observed that as monocular contrast sensitivity increases, the crowding effect decreases.[71] Early research has shown that crowding can occur dichoptically, but comparisons across studies are complicated by the selective nature of different types of stimuli (such as stimulus similarity, context, and attention).[72] A few pilot studies of binocular approaches have suggested that balancing the contrast gap between the eyes through dichoptic stimulation may reduce the crowding effect.[73] However, the lack of comprehensive research in this area hinders our understanding of how binocular approaches may alleviate

the crowding effect, thereby limiting their potential as effective interventions in visual rehabilitation.

Conclusion

Dichoptic-based binocular therapies present promising advances in the treatment of amblyopia by directly addressing binocular dysfunctions and promoting binocular vision. These approaches aim to reduce inhibitory interactions within the visual cortex, potentially improving stereoacuity and alleviating the crowding effect. Pilot studies have shown positive outcomes, but these findings remain unconfirmed by large-scale, multicenter randomized controlled trials. Key uncertainties persist regarding optimal contrast reduction, progression rates, and the duration of therapy once equal contrast is achieved. Additionally, the variability in amblyopia severity among patients highlights the need for personalized treatment protocols. While home-based treatment models could increase accessibility and patient reach, concerns about adherence and the reliability of self-administered therapy raise questions about their effectiveness. Furthermore, the potential for new-onset diplopia, though rare, remains a consideration due to the mechanisms of anti-suppression pathways involved. Despite these challenges, the development of dichoptic therapies holds significant promise for amblyopia treatment, particularly if future research addresses current limitations and further clarifies the mechanisms behind the crowding effect and its reduction.

Declarations

Authorship Contributions

Concept: D.Y., H.T.Ş., Design: D.Y., H.T.Ş., Data Collection or Processing: D.Y., H.T.Ş., Analysis or Interpretation: D.Y., H.T.Ş., Literature Search: D.Y., H.T.Ş., Writing: D.Y., H.T.Ş.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Wright KW. Binocular vision and introduction to strabismus. In: Wright KW, Yi Ning J, Strube YNJ, eds. Pediatric ophthalmology and strabismus 3rd ed. USA; Oxford University Press; 2012:231-247.
2. Fu VL, Norcia AM, Birch EE. Fusional suppression in accommodative and infantile esotropia. Invest Ophthalmol Vis Sci. 2006;47:2450.
3. Birch EE. Amblyopia and binocular vision. Prog Retin Eye Res. 2013;33:67-84.
4. Yıldız AA, Bardak Y. Effectiveness of patching in correcting refractive errors in cases with anisometropic amblyopia. Turk J Ophthalmol. 201;4:385-388.
5. Loudon SE, Simonsz HJ. The history of the treatment of amblyopia. Strabismus. 2005;13:93-106.
6. Repka MX, Beck RW, Holmes JM, Birch EE, Chandler DL, Cotter SA, Hertle RW, Kraker RT, Moke PS, Quinn GE, Scheiman MM; Pediatric Eye Disease Investigator Group. A randomized trial of patching regimens for treatment of moderate amblyopia in children. Arch Ophthalmol. 2003;121:603-611.
7. Holmes JM, Kraker RT, Beck RW, Birch EE, Cotter SA, Everett DF, Hertle RW, Quinn GE, Repka MX, Scheiman MM, Wallace DK; Pediatric Eye Disease Investigator Group. A randomized trial of prescribed patching regimens for treatment of severe amblyopia in children. Ophthalmology. 2003;110:2075-2087.
8. Stewart CE, Moseley MJ, Stephens DA, Fielder AR. Treatment dose-response in amblyopia therapy: the Monitored Occlusion Treatment of Amblyopia Study (MOTAS). Invest Ophthalmol Vis Sci. 2004;45:3048-3054.
9. Stewart CE, Stephens DA, Fielder AR, Moseley MJ; ROTAS Cooperative. Objectively monitored patching regimens for treatment of amblyopia: randomised trial. BMJ. 2007;335:707.
10. Vagge A, Gunton KB, Schnall B. A pilot study using electronic reminders for amblyopia treatment. Strabismus. 2018;26:184-190.
11. von Noorden GK, Campos EC. Patching regimens. Ophthalmology. 2004;111:1063-1066.
12. Somer D, Yabanoğlu D. Current refractive adaptation process and approach to patching treatment in amblyopia in light of studies monitoring patching time: traditional review. Turkiye Klinikleri J Ophthalmol. 2022;31:92-100.
13. Kushner BJ. Patching regimens for amblyopia. Ophthalmology. 2005;112:736-737.
14. Pediatric Eye Disease Investigator Group; Wallace DK, Lazar EL, Holmes JM, Repka MX, Cotter SA, Chen AM, Kraker RT, Beck RW, Clarke MP, Lorenzana IJ, Petersen DB, Roberts JT, Suh DW. A randomized trial of increasing patching for amblyopia. Ophthalmology. 2013;120:2270-2277.
15. Pediatric Eye Disease Investigator Group. Pharmacological plus optical penalization treatment for amblyopia: results of a randomized trial. Arch Ophthalmol. 2009;127:22-30.
16. Repka MX, Gallin PF, Scholz RT, Guyton DL. Determination of optical penalization by vectographic fixation reversal. Ophthalmology. 1985;92:1584-1586.
17. Pediatric Eye Disease Investigator Group. A randomized trial of atropine vs. patching for treatment of moderate amblyopia in children. Arch Ophthalmol. 2002;120:268-278.
18. Repka MX, Cotter SA, Beck RW, Kraker RT, Birch EE, Everett DF, Hertle RW, Holmes JM, Quinn GE, Sala NA, Scheiman MM, Stager DR Sr, Wallace DK; Pediatric Eye Disease Investigator Group. A randomized trial of atropine regimens for treatment of moderate amblyopia in children. Ophthalmology. 2004;111:2076-2085.
19. Pediatric Eye Disease Investigator Group; Repka MX, Kraker RT, Beck RW, Holmes JM, Cotter SA, Birch EE, Astle WF, Chandler DL, Felius J, Arnold RW, Tien DR, Glaser SR. A randomized trial of atropine vs patching for treatment of moderate amblyopia: follow-up at age 10 years. Arch Ophthalmol. 2008;126:1039-1044.
20. Agervi P, Kugelberg U, Kugelberg M, Simonsson G, Fornander M, Zetterström C. Treatment of anisometropic amblyopia with spectacles or in combination with translucent Bangerter filters. Ophthalmology. 2009;116:1475-1480.
21. Pediatric Eye Disease Investigator Group Writing Committee; Rutstein RP, Quinn GE, Lazar EL, Beck RW, Bonsall DJ, Cotter SA, Crouch ER, Holmes JM, Hoover DL, Leske DA, Lorenzana IJ, Repka MX, Suh DW. A randomized trial comparing Bangerter filters and patching for the treatment of moderate amblyopia in children. Ophthalmology. 2010;117:998-1004.
22. Polat U, Ma-Naim T, Belkin M, Sagi D. Improving vision in adult amblyopia by perceptual learning. Proc Natl Acad Sci U S A. 2004;101:6692-6697.
23. Chen PL, Chen JT, Fu JJ, Chien KH, Lu DW. A pilot study of anisometropic amblyopia improved in adults and children by perceptual learning: an alternative treatment to patching. Ophthalmic Physiol Opt. 2008;28:422-428.
24. Hess RF, Thompson B. Amblyopia and the binocular approach to its therapy. Vision Res. 2015;114:4-16.
25. Grant S, Moseley MJ. Amblyopia and real-world visuomotor tasks. Strabismus. 2011;19:119-128.
26. Kind PC, Mitchell DE, Ahmed B, Blakemore C, Bonhoeffer T, Sengpiel F. Correlated binocular activity guides recovery from monocular deprivation. Nature. 2002;416:430-433.
27. Baker DH, Meese TS, Mansouri B, Hess RF. Binocular summation of contrast remains intact in strabismic amblyopia. Invest Ophthalmol Vis Sci. 2007;48:5332-5338.

28. Mansouri B, Thompson B, Hess RF. Measurement of suprathreshold binocular interactions in amblyopia. Vision Res. 2008;48:2775-2784.
29. Hess RF, Mansouri B, Thompson B. A new binocular approach to the treatment of amblyopia in adults well beyond the critical period of visual development. Restor Neurol Neurosci. 2010;28:793-802.
30. Eastgate RM, Griffiths GD, Waddingham PE, Moody AD, Butler TK, Cobb SV, Comaish IF, Haworth SM, Gregson RM, Ash IM, Brown SM. Modified virtual reality technology for treatment of amblyopia. Eye (Lond). 2006;20:370-374.
31. Brown R, Blanchfield P, Fakis A, McGraw P, Foss AJE; I-BiT Study Group. Clinical investigation plan for the use of interactive binocular treatment (I-BiT) for the management of anisometropic, strabismic and mixed amblyopia in children aged 3.5-12 years: a randomised controlled trial. Trials. 2019;20:437.
32. Herbison N, Cobb S, Gregson R, Ash I, Eastgate R, Purdy J, Hepburn T, MacKeith D, Foss A; I-BiT study group. Interactive binocular treatment (I-BiT) for amblyopia: results of a pilot study of 3D shutter glasses system. Eye (Lond). 2013;27:1077-1083.
33. Waddingham PE, Butler TK, Cobb SV, Moody AD, Comaish IF, Haworth SM, Gregson RM, Ash IM, Brown SM, Eastgate RM, Griffiths GD. Preliminary results from the use of the novel interactive binocular treatment (I-BiT) system, in the treatment of strabismic and anisometropic amblyopia. Eye (Lond). 2006;20:375-378.
34. Herbison N, MacKeith D, Vivian A, Purdy J, Fakis A, Ash IM, Cobb SV, Eastgate RM, Haworth SM, Gregson RM, Foss AJ. Randomised controlled trial of video clips and interactive games to improve vision in children with amblyopia using the I-BiT system. Br J Ophthalmol. 2016;100:1511-1516.
35. Rajavi Z, Sabbaghi H, Amini Sharifi E, Behradfar N, Yaseri M. The role of interactive binocular treatment system in amblyopia therapy. J Curr Ophthalmol. 2016;28:217-222.
36. Rajavi Z, Sabbaghi H, Amini Sharifi E, Behradfar N, Kheiri B. Comparison between patching and interactive binocular treatment in amblyopia: a randomized clinical trial. J Curr Ophthalmol. 2019;31:426-431.
37. Xu JP, He ZJ, Ooi TL. Effectively reducing sensory eye dominance with a push-pull perceptual learning protocol. Curr Biol. 2010;20:1864-1868.
38. Ooi TL, Su YR, Natale DM, He ZJ. A push-pull treatment for strengthening the 'lazy eye' in amblyopia. Curr Biol. 2013;23:309-310.
39. Xu JP, He ZJ, Ooi TL. Push-pull training reduces foveal sensory eye dominance within the early visual channels. Vision Res. 2012;61:48-59.
40. Ooi TL, He ZJ. Sensory eye dominance: relationship between eye and brain. Eye Brain. 2020;12:25-31.
41. Shi W, He L, Lv B, Li L, Wu T. Evaluating the acute effect of stereoscopic recovery by dichoptic stimulation using electroencephalogram. Comput Math Methods Med. 2020;2020:9497369.
42. Vedamurthy I, Nahum M, Bavelier D, Levi DM. Mechanisms of recovery of visual function in adult amblyopia through a tailored action video game. Sci Rep. 2015;5:8482.
43. Bayliss JD, Vedamurthy I, Nahum M, Levi D, Bavelier D. Lazy eye shooter: making a game therapy for visual recovery in adult amblyopia usable. In: Marcus A. Design, User Experience, and Usability. Health, Learning, Playing, Cultural, and Cross-Cultural User Experience. Springer Berlin Heidelberg; 2013:352-360.
44. Vedamurthy I, Nahum M, Huang SJ, Zheng F, Bayliss J, Bavelier D, Levi DM. A dichoptic custom-made action video game as a treatment for adult amblyopia. Vision Res. 2015;114:173-187.
45. To L, Thompson B, Blum JR, Maehara G, Hess RF, Cooperstock JR. A game platform for treatment of amblyopia. IEEE Trans Neural Syst Rehabil Eng. 2011;19:280-289.
46. Knox PJ, Simmers AJ, Gray LS, Cleary M. An exploratory study: prolonged periods of binocular stimulation can provide an effective treatment for childhood amblyopia. Invest Ophthalmol Vis Sci. 2012;53:817-824.
47. Birch EE, Li SL, Jost RM, Morale SE, De La Cruz A, Stager D Jr, Dao L, Stager DR Sr. Binocular iPad treatment for amblyopia in preschool children. J AAPOS. 2015;19:6-11.
48. Li SL, Jost RM, Morale SE, Stager DR, Dao L, Stager D, Birch EE. A binocular iPad treatment for amblyopic children. Eye (Lond). 2014;28:1246-1253.
49. Li SL, Jost RM, Morale SE, De La Cruz A, Dao L, Stager D Jr, Birch EE. Binocular iPad treatment of amblyopia for lasting improvement of visual acuity. JAMA Ophthalmol. 2015;133:479-480.
50. Holmes JM, Manh VM, Lazar EL, Beck RW, Birch EE, Kraker RT, Crouch ER, Erzurum SA, Khuddus N, Summers AI, Wallace DK; Pediatric Eye Disease Investigator Group. Effect of a binocular iPad game vs part-time patching in children aged 5 to 12 years with amblyopia: a randomized clinical trial. JAMA Ophthalmol. 2016;134:1391-1400.
51. Manh VM, Holmes JM, Lazar EL, Kraker RT, Wallace DK, Kulp MT, Galvin JA, Shah BK, Davis PL; Pediatric Eye Disease Investigator Group. A randomized trial of a binocular iPad game versus part-time patching in children aged 13 to 16 years with amblyopia. Am J Ophthalmol. 2018;186:104-115.
52. Kelly KR, Jost RM, Dao L, Beauchamp CL, Leffler JN, Birch EE. Binocular iPad game vs patching for treatment of amblyopia in children: a randomized clinical trial. JAMA Ophthalmol. 2016;134:1402-1408.
53. Boniquet-Sanchez S, Sabater-Cruz N. Current management of amblyopia with new technologies for binocular treatment. Vision (Basel). 2021;5:31.
54. Kelly KR, Jost RM, Wang YZ, Dao L, Beauchamp CL, Leffler JN, Birch EE. Improved binocular outcomes following binocular treatment for childhood amblyopia. Invest Ophthalmol Vis Sci. 2018;59:1221-1228.
55. Pediatric Eye Disease Investigator Group; Holmes JM, Manny RE, Lazar EL, Birch EE, Kelly KR, Summers AI, Martinson SR, Raghuram A, Colburn JD, Law C, Marsh JD, Bitner DP, Kraker RT, Wallace DK. A randomized trial of binocular dig rush game treatment for amblyopia in children aged 7 to 12 years. Ophthalmology. 2019;126:456-466.
56. Manny RE, Holmes JM, Kraker RT, Li Z, Waters AL, Kelly KR, Kong L, Crouch ER, Lorenzana IJ, Alkharashi MS, Galvin JA, Rice ML, Melia BM, Cotter SA; Pediatric Eye Disease Investigator Group. A randomized trial of binocular dig rush game treatment for amblyopia in children aged 4 to 6 years. Optom Vis Sci. 2022;99:213-227.
57. Blaha J, Gupta M. Diplopia: a virtual reality game designed to help amblyopics. IEEE Virtual Reality (VR). 2014:163-164.
58. Žiak P, Holm A, Halička J, Mojžiš P, Piñero DP. Amblyopia treatment of adults with dichoptic training using the virtual reality oculus rift head mounted display: preliminary results. BMC Ophthalmol. 2017;17:105.
59. Aderman CM, Deiner M, Gupta M, Blaha J, Levin MH. Dichoptic virtual reality therapy for amblyopia in adults. Invest Ophthalmol Vis Sci. 2015;56:2191.
60. Dużmańska N, Strojny P, Strojny A. Can simulator sickness be avoided? A review on temporal aspects of simulator sickness. Front Psychol. 2018;9:2132.
61. Li SL, Reynaud A, Hess RF, Wang YZ, Jost RM, Morale SE, De La Cruz A, Dao L, Stager D Jr, Birch EE. Dichoptic movie viewing treats childhood amblyopia. J AAPOS. 2015;19:401-405.
62. Birch EE, Jost RM, De La Cruz A, Kelly KR, Beauchamp CL, Dao L, Stager D Jr, Leffler JN. Binocular amblyopia treatment with contrast-rebalanced movies. J AAPOS. 2019;23:160.
63. Sauvan L, Stolowy N, Denis D, Matonti F, Chavane F, Hess RF, Reynaud A. Contribution of short-time occlusion of the amblyopic eye to a passive dichoptic video treatment for amblyopia beyond the critical period. Neural Plast. 2019;2019:6208414.
64. Bossi M, Tailor VK, Anderson EJ, Bex PJ, Greenwood JA, Dahlmann-Noor A, Dakin SC. Binocular therapy for childhood amblyopia improves vision without breaking interocular suppression. Invest Ophthalmol Vis Sci. 2017;58:3031-3043.
65. Xiao S, Angjeli E, Wu HC, Gaier ED, Gomez S, Travers DA, Binenbaum G, Langer R, Hunter DG, Repka MX; Luminopia Pivotal Trial Group. Randomized controlled trial of a dichoptic digital therapeutic for amblyopia. Ophthalmology. 2022;129:77-85.
66. Jost RM, Hudgins LA, Dao LM, Stager DR Jr, Luu B, Beauchamp CL, Hunter JS, Giridhar P, Wang YZ, Birch EE. Randomized clinical trial of streaming dichoptic movies versus patching for treatment of amblyopia in children aged 3 to 7 years. Sci Rep. 2022;12:4157.

67. Xiao S, Gaier ED, Mazow ML, Stout AU, Travers DA, Angjeli E, Wu HC, Binenbaum G, Hunter DG. Improved adherence and treatment outcomes with an engaging, personalized digital therapeutic in amblyopia. Sci Rep. 2020;10:8328.
68. Xiao S, Gaier ED, Wu HC, Angjeli E, Nuth PL, Bohra LI, Miller AM, Mazow ML, Stout AU, Morse CL, Blumenfeld LC, Glaser SR, Crouch E, Ekdawi NS, Lyon DW, Silbert DI, Hunter DG. Digital therapeutic improves visual acuity and encourages high adherence in amblyopic children in open-label pilot study. J AAPOS. 2021;25:87.
69. Li J, Spiegel DP, Hess RF, Chen Z, Chan LY, Deng D, Yu M, Thompson B. Dichoptic training improves contrast sensitivity in adults with amblyopia. Vision Res. 2015;114:161-172.
70. Masgoret X, Asper L, Alexander J, Suttle C. The development of crowding and interocular interactions in a resolution acuity task. Invest Ophthalmol Vis Sci. 2011;52:9452-9456.
71. Barollo M, Contemori G, Battaglini L, Pavan A, Casco C. Perceptual learning improves contrast sensitivity, visual acuity, and foveal crowding in amblyopia. Restor Neurol Neurosci. 2017;35:483-496.
72. Whitney D, Levi DM. Visual crowding: a fundamental limit on conscious perception and object recognition. Trends Cogn Sci. 2011;15:160-168.
73. Hernández-Rodríguez CJ, Piñero DP, Molina-Martín A, Morales-Quezada L, de Fez D, Leal-Vega L, Arenillas JF, Coco-Martín MB. Stimuli characteristics and psychophysical requirements for visual training in amblyopia: a narrative review. J Clin Med. 2020;9:3985.