

A review of the treatment of anisometropic amblyopia in adults using dichoptic therapy



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Background: In recent years, it has been established that the suppression of the amblyopic eye by the fellow eye is the major cause of amblyopia. New behavioural therapies like dichoptic therapy attempt to reduce suppression in amblyopic adults who have passed the critical stage of visual cortex development. Anisometropic amblyopia has the highest prevalence of amblyopia, and managing this condition in adults may lead to improvement in the quality of life.

Aim: The purpose of the review is to assess the impact of this novel treatment of amblyopia, with particular focus on using dichoptic therapy for anisometropic amblyopia in adults.

Methods: A literature search was conducted on articles published in the last 20 years, and papers were sourced from databases such as Elsevier, Science Direct and PubMed using the reference manager Mendeley. (The search was performed from December 2017 to December 2018.)

Results: Evidence from located studies in adults with anisometropic or mixed amblyopia managed with new behavioural treatments including dichoptic therapy showed some significant improvement in the best-corrected distance visual acuity, stereopsis and contrast sensitivity whilst improving or restoring optimal binocular vision.

Conclusion: Adults with anisometropic and/or mixed amblyopia can benefit from dichoptic therapy with a unique approach to improve binocularity concurrently. The therapy represents a viable option for managing amblyopia in adults and can be administered as office-based or home-based treatment in a timely manner that could improve the quality of life for such patients.

Keywords: amblyopia; adult anisometropic amblyopia; binocular vision; contrast sensitivity; stereo-acuity; visual acuity; dichoptic therapy.

Introduction

Dichoptic therapy targets suppression directly, which results in a significant improvement in both monocular and binocular visual functions in adults with anisometropic amblyopia.¹ Historically, amblyopia was believed to be a monocular disorder which leads to a binocular dysfunction. Apart from refractive error, amblyopia is considered the most frequent cause of vision loss in infants and young children, affecting about 1% – 4% of the world's population.^{2,3,4,5,6,7} Amblyopia if left untreated extends into adulthood and may impact livelihoods of those affected. Amblyopic sufferers also experience a broad range of low- and high-level visual deficits, including contrast sensitivity reduction,⁸ high level of spatial uncertainty,⁹ poor monocular fixation,¹⁰ higher sensitivity to contour interaction effect^{11,12} and impaired reading abilities.¹³ Traditionally, it was believed that the visual deficits in amblyopia could be reversed only if its treatment was administered before the end of the critical period of visual cortex maturation. However, this reversal was usually possible up to 13 years of age, which was often achieved using the standard treatment: monocular occlusion and atropine penalisation.¹⁴ Amblyopia is characterised by a number of visual deficits that influence both monocular and binocular visual functions.¹⁵ These deficits were interpreted as amblyopia which is anatomically monocular without any evidence of binocular function. However, recent findings have provided strong evidence of intact binocular mechanisms in adult amblyopes which may have been lost but were, in fact, suppressed under binocular viewing.¹⁶

Visual cognition is important in activities of daily living; however, in amblyopes, this cognitive ability is abnormal. Wang et al. found that in amblyopia, both the amblyopic and fellow eyes are abnormal midway and at the end stage of cognitive processing during the developmental stage.¹⁷ Recent behavioural treatment methods such as perceptual learning, video gaming and dichoptic

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training are proposed by some researchers to improve visual functions in adults suffering from various forms of amblyopia.¹⁴ The monocular treatment for amblyopia was for the purpose of improving visual performance of the amblyopic eye. Nevertheless, it is now argued by several researchers that this treatment approach may not be maximally effective as it does not directly address suppression. Therefore, it is considered ineffective in adults who have passed the critical period of visual cortex development.^{2,14,18} Because of this fact, amblyopia is alternatively considered as a binocular problem. In cases of binocular amblyopia such as isoametropic amblyopia, both eyes are visually impaired, and in monocular amblyopia, the impaired vision of one eye leads to a binocular dysfunction. Therefore, considering these facts, amblyopia can generally be considered a binocular problem.

There is a presupposition that in amblyopia, the loss of visual function in one eye is the primary problem and that the loss of binocular vision is the secondary consequence. However, an alternative argument is to consider the loss of binocular vision as the primary problem leading to amblyopia.^{2,19} Therefore, if the latter is the case, the main aim of treating amblyopia will then be to treat the binocular disorder caused by the suppression of the amblyopic eye via the non-amblyopic eye in the case of monocular amblyopia or binocular deprived vision in the case of binocular amblyopia. This process can be achieved using the new behavioural therapies.^{20,21}

Among the various forms of amblyopia, anisometropic amblyopia has the highest prevalence of 61.6% of all cases of amblyopia.²² The amblyogenic risk factors in terms of uncorrected unequal refractive errors in both eyes are a difference of astigmatism > 1.50 dioptre (D), hyperopia > 1 D and myopia with magnitude $> | -3 |$ D.²³ Anisometropic amblyopia may commonly occur alongside strabismic amblyopia, termed mixed amblyopia, but these types can be differentiated using clinical routine examination.²⁴ Anisometropic amblyopia is thought to result partially from direct effects of image blur on the development of visual acuity in the amblyopic eye and partially from direct inter-ocular rivalry or inhibition similar to strabismic amblyopia.²⁵

In most adults with anisometropic amblyopia, the degree of anisometropic amblyopia is large and is because of long-standing uncorrected anisometropia.²⁶ Leon et al.²⁷ propounded that there are possibilities of an increase in anisometropic amblyopia both during infancy and with more severe anisometropic amblyopia during early childhood. Anisometropic amblyopia severity and onset is difficult to address in childhood because it involves both prevalence of a condition that is not evidently easy to detect as there is no manifest ocular misalignment and the amblyopia may go undetected because of the challenges of measuring visual acuity during infancy.²⁸ These reasons along with inadequate school vision screening programmes could perhaps account for the high prevalence of anisometropic amblyopia among other forms of amblyopia that have affected mainly young adults because of the failure of early detection.

Dichoptic therapy is a behavioural therapy for managing amblyopia where the two eyes are made to work concomitantly and independently. This is achieved by dissociation and contrast re-balancing. The therapy can consist of stimuli of two separate colours viewed through a digital screen whilst wearing either a lenticular overlay or an anaglyphic red-green filter which helps dissociating the images seen by the two eyes.¹⁹ Previous reports of dichoptic training of adult amblyopes were conducted in a clinic-based setting, thus showing reliability as well as the potential for improving amblyopia beyond the critical period of visual cortex development.²⁹ Binocular approaches to manage amblyopia have shown improvement in stereopsis and visual acuity both in children and in adults.³⁰ One of these approaches involved dichoptic therapy that encouraged binocular fusion for the purpose of completing a task. This therapy originated from the idea that amblyopia is basically a binocular disorder embedded in inter-ocular suppression and that successful treatment should involve the use of both eyes.³¹ With this therapy, participants suffering from amblyopia are trained on tasks where stimuli are presented in a dichoptic manner. In this method of therapy, the contrast of the image seen by the non-amblyopic eye is diminished to encourage binocular fusion of the two inputs. With time, the contrast in the fellow eye is increased until uniform contrast is attained for both eyes. This is the principle of dichoptic therapy. The earlier task was a *motion coherent* task where the participant distinguishes the direction of motion of signal dots among background noise dots, mostly with signal dots introduced to one eye and noise dots to the other eye.³¹ Later, a game using bricks named *Tetris* was developed in which bricks separated in two colours (red and green) were presented independently. This was achieved by wearing anaglyphic red-green filters, and the eye with the red filter could see the red bricks and the eye with the green filter could see the green bricks. By reducing the contrast on the fellow eye bricks, the signals from the two eyes could be fused so as to play the game successfully.^{18,32,33} This is the technique used by dichoptic therapy to treat amblyopia. The method was validated and dichoptic therapy improved visual acuity and, in some cases, stereo-acuity in amblyopes by reducing inter-ocular suppression, making it possible for both monocular and binocular vision functions to improve.³⁴

Dichoptic therapy has shown that there is a proximate relationship between suppression and anisometropic amblyopia. Therefore, there are suggestions related to the management of loss of binocular vision because of anisometropic amblyopia, with the expectation of reducing or eliminating the suppression of the amblyopic eye. This process leads to the reinforcement of binocularity.¹ Research^{35,36} has shown that the binocular function in amblyopic adults is not permanently lost and could be improved through specialised behavioural training using dichoptic therapy,^{29,31} and binocular dichoptic therapy is more effective than its monocular form.

Anisometropic amblyopia is believed, by most researchers, to be a cortical impairment because of an abnormal visual

experience in early childhood, leading to a difference in refractive power in the two eyes.³⁷ Over time, as this is left untreated, chronic blur on one or both retinæ causes unequal focus between the two eyes, leading to the suppression of the more blurred eye.³⁸ The process of vision occurs as a neural coding that is transferred from the thalamus, from the cells of the lateral geniculate nucleus to those of the visual cortex. The visual cortex is located in the occipital lobe at the calcarine sulcus where excitatory and inhibitory binocular convergence takes place. A fragmented representation of scene and object is integrated in cortical synaptic connections that create a recognisable visual image. Changes in the morphophysiology associated with the abnormalities of visual processing cause amblyopia.³⁹ In monocular visual deprivation, visual impairment occurs as a result of a conflict between the neural systems of the two eyes in terms of their influence on cortical neurons. Input from the eye with a higher capacity to perceive vision therefore suppresses the input from the other eye, leading to amblyopia.⁴⁰

The *Tetris* application has been designed and made available in the Apple app-store, and there is also an Android version of the software. The benefit of this therapy is that it can be done in the comfort of one's own home using a mobile device. With the introduction of dichoptic therapy and other behavioural therapies, the response rate and duration of therapy as compared to conventional patching have been reduced. With dichoptic therapy, the amblyopic patient is said to notice a remarkable improvement within 10–40 hours of training time as compared to monocular patching in children where improvement is noticed after 17 weeks of patching.⁴¹ Dichoptic therapy has also helped in eliminating any emotional stress that comes with wearing an eye patch in public. In patching, improvement of the visual acuity of the amblyopic eye is the target, but in dichoptic therapy, improvement in binocular vision is the primary objective.

The aim of this review is to assess the impact of this novel treatment in adults with anisometropic, strabismic and mixed amblyopia, with a particular focus on anisometropic amblyopia. This is achieved through examination of the evidence for success with this form of treatment beyond the critical or sensitivity period to reduce the burden of visual loss in the age group that primarily contributes to the economies of countries worldwide.

Methods and scope of review

A comprehensive literature search using electronic databases was conducted between December 2017 and December 2018. Databases including Elsevier, Science Direct, Research Gate and PubMed were used to source scientific publications using the reference manager Mendeley.

Keywords utilised in these searches included 'amblyopia', 'anisometropia', 'binocular vision', 'contrast sensitivity', 'stereo acuity', 'visual acuity' and 'dichoptic therapy'. Pertinent articles on reference lists were established and

recovered from electronic and print journals. The majority of the reviewed articles were obtained electronically by the aforementioned search engines.

For the current review, studies were first profiled separately, followed by comparisons and combination with other related studies notwithstanding the classification criteria, measurement proficiencies and source of variations; and limitations of the studies were discussed. This review is on the treatment of adults who suffer from anisometropic amblyopia, with the focus on the use of dichoptic therapy. Studies related to the management of amblyopia in children using the standard occlusion therapies were excluded from the search. Non-peer-reviewed scientific articles were also excluded. There was specific interest on anisometropic amblyopia in adults, management of amblyopia in adults and the use of dichoptic therapy in treating amblyopia.

Ethical considerations

Ethical clearance was issued by Biomedical Research Ethics Administration, Research Office, Westville Campus (ethical clearance number: BE704/18).

Results

The treatment of amblyopia in this review is based on the finding that if the contrast in the fellow eye is gradually reduced, depending on the severity of the suppression, a level will be reached where the information is combined by both eyes causing equality in contrast. The attainment of this equality in contrast is a direct relationship between the strength of suppression and the depth of amblyopia.^{23,25,42} This can be explained based on the effect of dichoptic therapy on certain visual functions, including visual acuity, stereo-acuity and contrast sensitivity in anisometropic, strabismic and mixed amblyopia which accounts for a combination of both anisometropic and strabismus amblyopia. Hess et al.⁴³ in their study on amblyopia and the binocular approach to its therapy found that binocular therapies for treating amblyopia in adults had no adverse effects, such as diplopia. This may be because of the fact that the therapies are done under conditions where both eyes are operational.

From various studies provided in the tables below, it was found that the age groups used for the studies were between 13 and 66 years, who had passed the critical stage of visual development. It was found that regardless of age, various dichoptic therapies showed similar levels of improvement in visual functions. Duration of training was not a significant factor in the improvement of visual functions. From Table 1, it was shown that different studies used different durations but arrived at similar improvement in stereo-acuity, distant acuity and contrast sensitivity. In 2013, Li et al.³³ demonstrated that the effect produced after 40 hours of clinic-supervised training with dichoptic therapy could also be achieved, or even more, after just 10 h of the same training.

Dichoptic therapy and visual acuity improvement in anisometropic, strabismic and mixed amblyopes

The pre- and post-therapy distance visual acuity (DVA) measurements in previous studies in Table 1 indicate the estimated changes in visual acuity (VA) from studies that included the use of dichoptic therapy on adults with anisometropic, strabismic and mixed amblyopia. The administrations of most of the dichoptic therapies were clinic-based. However, the findings of the study conducted by Hess et al.¹ showed that with home-based dichoptic therapy alone, using the iPod device showed a remarkable improvement in VA from 0.52 LogMAR to 0.27 LogMAR, which is approximately three lines of improvement. Likewise, Li et al.³³ compared monocular game play with dichoptic game play and found that dichoptic game play improved VA from 0.52 LogMAR to 0.36 LogMAR (thus a 0.16 LogMAR gain) compared to monocular game play which gained only 0.05 LogMAR (from 0.52 LogMAR to 0.47 LogMAR). In support of the findings of the studies conducted by Hess and Li, Vedomurthy et al.⁴¹ found that monocular watching of action movies only improved VA by 0.15 LogMAR as compared to a greater improvement by 0.21 LogMAR with dichoptic playing of action games. Comparing the different types of amblyopia such as anisometropic and strabismic, it was also discovered that after the first 13 h of therapy, anisometropic amblyopes in the game group showed a similar VA improvement as that of strabismic amblyopia: 0.08 LogMAR or approximately 15.7% and 0.08 LogMAR or 15.8%, respectively, whereas in the movies group, anisometropic amblyopes showed a greater improvement by 0.08 LogMAR or 16.6% as compared

to strabismic amblyopes of the same movie group with improvement of only 0.02 LogMAR or 4.8%. Table 1 shows that regardless of the duration of exposure to dichoptic therapy, there was almost the same level of VA improvement across studies. Li et al.³³ using only dichoptic therapy as compared to Spiegel et al.⁴² who combined dichoptic therapy with transcranial direct current stimulation (tDCS) showed no significant difference in the improvement in VA. Long et al.¹⁹ found that with clinic-based dichoptic therapy on adults, the change in VA was significant with a pre-treatment from 0.53 LogMAR to a post-treatment of 0.36 LogMAR. Similarly, the same was observed in a home-based study by Hess et al.,¹ with an improvement in VA from 0.52 to 0.36 LogMAR. Also, in Hess et al.'s study,³² dichoptic treatment was administered in the clinic, and the findings were compared to home-based therapy by Hess et al.¹, showing that home-based outcomes were as good as previously reported clinic-based result.

Dichoptic therapy and stereo-acuity improvement in anisometropic, strabismic and mixed amblyopia

Changes in stereo-sensitivity, which is a measure of the depth perception, of individuals with good binocular vision were considered in seven studies. Stereo-acuities were converted to stereo-sensitivities (using the formula stereo-sensitivity = stereo-acuity⁻¹) as the stereopsis of many patients could not be measured prior to treatment. Table 2 shows the pre- and post-stereo-sensitivities of amblyopic adult participants using dichoptic therapy, whilst some studies compared dichoptic therapy with other therapies. The findings of various studies as shown in Table 2 provide support that

TABLE 1: Dichoptic therapy and distance visual acuity improvement in anisometropic, strabismic and mixed amblyopes.

Study	Article title	Modality	N	Age (years)	Amblyopia type (n)	Dichoptic therapy medium/(n)	Duration (hrs)	Change in DVA (LogMAR)	
								Pre	Post
Hess et al. ³¹	A new binocular approach to the treatment of amblyopia in adults well beyond the critical period of visual development	Clinic-based	9	24–49	Strabismic (7) Mixed (2)	Dichoptic Global motion <i>Stereoscope</i>	16–24	0.50	0.30
Li et al. ³³	Dichoptic training enables the adult amblyopic brain to learn	Clinic-based	18	19–26	Anisometropic Strabismic Mixed	Monocular Falling blocks <i>Head mounted video goggles</i> (9)	10	0.52	0.47
					Anisometropic Strabismic Mixed	Dichoptic Falling blocks <i>Head mounted video goggles</i> (9)	10	0.52	0.36
Long et al. ¹⁹	A game platform for the treatment of amblyopia	Clinic-based	9	17–51	Anisometropic Strabismic Mixed	Falling blocks <i>iPod/ Lenticular overlay</i>	6–35	0.54	0.36
Spiegel et al. ⁴²	Transcranial direct current stimulation enhances recovery of stereopsis in adults with amblyopia	Clinic-based	16	17–31	Anisometropic (9) Strabismic (6) Mixed (1)	Falling blocks Transcranial direct current stimulation (tDCS) <i>iPod/ Lenticular overlay</i>	10	0.64	0.30
Hess et al. ¹	The iPod binocular home-based treatment for amblyopia in adults: Efficacy and compliance	Home-based	14	13–50	Anisometropic (6) Strabismic (6) Mixed (2)	Falling blocks <i>iPod/ lenticular overlay/anaglyph</i>	10–30	0.525	0.36
Li et al. ⁴⁴	Dichoptic training improves contrast sensitivity in adults with amblyopia	Clinic-based	30	17–31	Anisometropic (20) Strabismic (9) Mixed (1)	Monocular Video goggles	10	0.52	0.47
						Dichoptic Video goggles	10	0.52	0.36
						Dichoptic video game <i>iPod/tDCS</i>	10	0.64	0.30
Vedomurthy et al. ⁴¹	A dichoptic custom-made action video game as a treatment for adult amblyopia	Clinic-based	38	19–66	Anisometropic (6) Strabismic (9)	Monocular Action TV Series <i>Computer monitor</i> (15)	40	0.58	0.43
					Anisometropic (10) Strabismic (13)	Dichoptic/custom-made unreal tournament VGP <i>Gamma corrected monitor</i> (23)	40	0.58	0.37

DVA, distance visual acuity.

dichoptic therapy is a viable method for improving stereo-acuity in adults with anisometropic, strabismic and mixed amblyopia. Li et al.³³ discovered that there was a greater improvement in stereo-sensitivity using dichoptic training than from monocular training. Dichoptic training improved stereo-sensitivity by a factor of 4, whilst monocular training had no significant improvement. Vedomurthy et al.⁴¹ compared monocular viewing of an action movie with the amblyopic eye to a dichoptic action game and discovered that there was a significant improvement in stereo-acuity by an average of 34% with the usage of the dichoptic game compared to an average of 17% for the monocular movie group. The participants with anisometropic amblyopia in the dichoptic game group were found to show the largest improvements of 46% compared to other participants in the same group, such as strabismic amblyopes (12.3%). In the group watching the movies with monocular vision, the anisometropic amblyopia had a lesser improvement of 21%, whilst strabismic amblyopia improved by 15%.⁴¹

Irrespective of the duration of exposure to dichoptic therapy, there was an improvement in stereo-acuity in the seven studies in the literature review. The changes in stereo-acuities with home-based dichoptic therapy were similar to those obtained in the clinic-based settings (see Table 2). This suggests that the home-based treatment of amblyopia in adults represents a viable option for the treatment of adults with anisometropic amblyopia,¹ and dichoptic therapy plays a greater role in improving stereo-acuity as compared to monocular therapy.

Dichoptic therapy and contrast sensitivity improvement in anisometropic, strabismic and mixed amblyopes

Table 3 shows the mean improvement in contrast sensitivity function using dichoptic and monocular therapy. Li et al.³³ measured the changes in contrast sensitivity using dichoptic therapy under monocular and binocular (dichoptic) conditions and observed that the dichoptic training in a

TABLE 2: Dichoptic therapy and stereo-sensitivity improvement in anisometropic, strabismic and mixed amblyopes.

Study	Article title	Modality	N	Age (years)	Amblyopia type (n)	Dichoptic therapy medium (n)	Duration (hours)	Stereo-sensitivity (Secs of arc ⁻¹)	
								Pre	Post
Hess et al. ³¹	A new binocular approach to the treatment of amblyopia in adults well beyond the critical period of visual development	Lab-based	9	24–49	Strabismic (7) Mixed (2)	Dichoptic Global motion Stereoscope	16–24	0.00220	0.0220
Long et al. ¹⁹	A game platform for the treatment of amblyopia	Lab-based	9	17–51	Anisometropic Strabismic Mixed	Falling blocks <i>Head-mounted video goggles</i>	6–35	0.00048	0.0086
Li et al. ³³	Dichoptic training enables the adult amblyopic brain to learn	Lab-based	18	19–26	Anisometropic Strabismic Mixed	Monocular Falling blocks <i>Head-mounted video goggles</i> (9)	10	0.00043	0.0007
					Anisometropic Strabismic Mixed	Dichoptic Falling blocks <i>iPod/Lenticular overlay</i> (9)	10	0.00043	0.0021
Spiegel et al. ⁴²	Transcranial direct current stimulation enhances recovery of stereopsis in adults with amblyopia	Lab-based	16	17–31	Anisometropic (9) Strabismic (6) Mixed (1)	Falling blocks Transcranial direct current stimulation (tDCS) <i>iPod/Lenticular overlay</i>	10	0.00031	0.0027
Hess et al. ¹	The iPod binocular home-based treatment for amblyopia in adults: Efficacy and compliance	Home-based	14	13–50	Anisometropic (6) Strabismic (6) Mixed (2)	Falling blocks <i>iPod/lenticular overlay and anaglyph</i>	10–30	0.00072	0.0030
Li et al. ⁴⁴	Dichoptic training improves contrast sensitivity in adults with amblyopia	Lab-based	30	17–31	Anisometropic(20) Strabismic (9) Mixed (1)	Video game Monocular Video goggles (9)	10	0.00042	0.0028
						Video game <i>Dichoptic Video goggles</i> (6)	10	0.00042	0.0021
						Dichoptic video game <i>iPod/tDCS</i> (15)	10	0.00025	0.0022
Vedomurthy et al. ⁴¹	A dichoptic custom-made action video game as a treatment for adult amblyopia	Lab-based	38	19–66	Anisometropic(6) Strabismic (9)	Monocular Action TV Series <i>Computer monitor</i>	40	0.00010	0.0009
					Anisometropic(10) Strabismic (13)	Dichoptic/custom-made unreal tournament VGP <i>Gamma corrected monitor</i>	40	0.00023	0.0023

VGP, videogame play; Secs, seconds.

TABLE 3: Dichoptic therapy and contrast sensitivity improvement in anisometropic, strabismic and mixed amblyopes.

Study	Article title	Modality	N	Age (years)	Amblyopia type (n)	Amblyopia intervention		Mean improvement in contrast sensitivity (log units)
						Intervention therapy device	Duration (hours)	
Li et al. ⁴⁴	Dichoptic training improves contrast sensitivity in adults with amblyopia	Lab-based	30	17–31	Anisometropic (20) Strabismic (9) Mixed (1)	Dichoptic Video game Monocular Video goggles	10	0.1 (SE 0.07)
						Dichoptic Video game <i>Dichoptic video goggles</i>	10	0.2 (SE 0.09)
						Dichoptic video game <i>iPod/tDCS</i>	10	No significant effect
Vedomurthy et al. ⁴¹	A dichoptic custom-made action video game as a treatment for adult amblyopia	Lab-based	38	19–66	Anisometropic (6) Strabismic (9)	Monocular watching of action TV Series <i>Computer monitor</i>	40	0.1
					Anisometropic (10) Strabismic (13)	Dichoptic/custom-made unreal tournament VGP <i>Gamma corrected monitor</i>	40	0.3

SE, standard error; VGP, videogame play.

binocular condition resulted in a significantly greater mean improvement of 0.2 log units compared to dichoptic training in a monocular condition which gave a mean improvement of 0.1 log units. This suggests that dichoptic therapy where the two eyes function independently is also more effective in improving contrast sensitivity than dichoptic training under monocular condition.

Vedamurthy et al.⁴¹ also showed similar contrast sensitivity changes by comparing monocular movie watching using the amblyopic eye and a videogame play (VGP) tournament version of dichoptic therapy. The findings showed a greater improvement in contrast sensitivity for the dichoptic video game group, with an average increase of 0.3 log units as compared to the monocular movie group that gained only 0.1 log units improvement. A pronounce improvement was detected in anisometropic patients who played the dichoptic videogame, with a contrast sensitivity change from 1.68 to 2.2 log units as compared to changes in other groups; from 1.8 to 1.9 log units for the anisometropic amblyopes who watched movies monocularly, from 2.2 to 2.4 log units for the dichoptic videogame group with strabismic amblyopia and from 1.9 to 1.96 log units for the monocular movies group participants with strabismic amblyopia.⁴¹

Participants with anisometropic amblyopia had the most gains with minimal duration to cause improvement in contrast sensitivity after 10 h of therapy.

Discussion

Dichoptic therapy was observed to induce a significant improvement in distant VA, stereo-acuity and contrast sensitivity in adults with anisometropic or mixed amblyopia, and more so in anisometropic amblyopic participants. Recent studies found that dichoptic therapy in a binocular condition may result in significant better learning effects than monocular training.^{33,44} Li et al.³³ demonstrated that just 10 h of playing dichoptic video games improved VA by more than 0.16 LogMAR. With *Tetris* dichoptic game therapy, an increase of 0.34 LogMAR in VA was reported by Spiegel et al.⁴² Dissimilar findings were reported using monocular video game play with patching of the non-amblyopic eye where VA in adults with amblyopia improved by an average of 0.05 LogMAR after 10 h of game play.³³ This comparison between monocular and binocular dichoptic training in adult amblyopia requires further investigation, especially in controlled studies.

The improvement among anisometropic amblyopes was demonstrated primarily in a clinic or office-based modality, with one study showing comparable results in a home-based setting. No adverse effects have been reported from the use of dichoptic therapy performed in binocular condition in training adults with amblyopia and with minimal risk of diplopia as dichoptic therapy conditions occur when fusion is operational.⁴³

A possible clinical concern is the likelihood of intractable diplopia that could be influenced by reducing inter-ocular

suppression without the presence of fusion; however, as dichoptic therapy was performed in a binocular condition, fusion is induced and the concern of diplopia is eliminated.⁴⁵ This is not applicable to occlusion therapy where reduced inter-ocular suppression may improve VA, without intact binocular circuitry, with participants at risk of having diplopia that cannot be improved by traditional means like strabismus surgery and/or prisms correction. However, there is evidence that dichoptic therapy does not induce diplopia,¹⁹ which has been reported to occur after the use of occlusion therapy in adults.⁴⁶

All the approaches utilised in these studies were limited to patients with anisometropic and strabismic amblyopia, with a small angle of strabismus below 10^Δ with an improvement in stereo-acuity and distant VA after a maximum time of 40 h and a post-therapy measurement up to 6 months to assess the possibility of amblyopia reversal.¹ Fewer studies^{7,20,44} have addressed the changes in contrast sensitivity as it was altered to effect rebalancing of binocular vision.

Using the traditional methods of managing amblyopia, such as patching and atropine penalisation, only monocular functions were found to improve. However, from the latest discoveries, it was validated that vision therapy treated the binocular anomalies such as convergence insufficiency, convergence excess, exotropia and esotropia among others which accompanies amblyopia, and it was found to be more effective than occlusion therapy alone.⁴⁷ Although not explored here, dichoptic vision therapy was found to focus on improving accommodation and enhancing oculomotor skills accuracy. In anisometropic, strabismic and mixed amblyopes, it was found that vergence ranges increased, whilst suppression and eccentric fixation reduced.⁴⁸

Hybrid-binocular methods are increasing in popularity, as these are aiming towards recovering monocular functions not under monocular conditions but under binocular viewing. In these approaches, the primary aims were to restore binocular fusion and stereopsis with an expected secondary consequence of improving vision of the amblyopic eye.

The role of age

Age has always been implicated as a significant factor in the effective treatment of amblyopia in children.^{49,50} Therefore, it is logical to speculate age to be an important factor in the effective treatment of amblyopia irrespective of age. This review study suggests that age may not have a significant effect on the outcomes of VA, stereo-acuity and contrast sensitivity in adults using dichoptic therapy. The age group regardless gained a remarkable improvement with dichoptic therapy, but more studies on the effect of dichoptic therapy on age will need to be carried out to be able to ascertain this fact. This evidence suggests that the visual cortex of adults still retains its plasticity into adulthood, which is supported by the confirmation of plasticity in visual attention and learning in normal vision and that dichoptic therapy could be used to rehabilitate

visual perception in adults with anisometropic, strabismic and mixed amblyopia within a short period of time.^{51,52}

Training duration

The review discovered that training duration was not an important factor in VA, stereo-acuity and contrast sensitivity improvement. Over a few weeks of using dichoptic therapy, binocular fusion could be extended to all contrasts even when the fellow eye was viewing stimuli naturally. Therefore, the important question is as follows: is there a minimal duration required for anisometropic or mixed amblyopia treatment using dichoptic therapy? To answer this question, improvement in visual outcomes using dichoptic therapy would have to be systematically monitored in a comprehensive clinical trial.

The duration of any particular type of therapy, dichoptic therapy, perceptual learning or video gaming, may not matter. However, considering the duration of use and the need for compliance with these therapies compared to occlusion therapy, treatments that require shorter durations would be a better option.

Although no known side effects are associated with these therapies, caution should be put in place whilst using them as none of them have been standardised, and a large clinical control trial is yet to be carried out.

Amblyopia types

From our review, it was shown that participants with different amblyopia types demonstrated distinct patterns of deficits.^{33,41} Studies have shown that strabismic and mixed amblyopia had poorer outcomes when compared to anisometropic amblyopia using dichoptic therapy. This could be as a result of the different degrees of suppression which could influence the amount of binocularity that exists in these various amblyopes, making the effect of dichoptic therapy to differ across these various types of amblyopia.⁵³ From the reviews, we do not have clear evidence of the efficient standard used in dichoptic training for dissociating the stimuli between the amblyopic eye and good eye; however, comparable results were found in a study between lenticular and anaglyphic platforms.^{1,54}

Limitations recognised in studies

It is notable that the majority of previous studies in this area were conducted in clinic-based settings, with limited evidence of home-based therapy. Therefore, the home-based therapy approach is important for future researchers to ascertain its advantages and disadvantages, if any, over clinic-based therapy. The review shows that distance VA, stereo-acuity and contrast sensitivity improved using the new treatments, dichoptic, perceptual learning and video gaming in adults, but little is known about the use of dichoptic therapy in children. However, with varied study designs, there is a need for a standard design in future

research. With dichoptic therapy, a standard and intensive training duration is required for optimal results, especially in cases with severe amblyopia. There is a need to recruit a large number of participants in future studies to reduce the risk of accidental bias or extreme outliers. Most of the studies in the literature review lacked control groups. Future studies need to recognise the importance of controls with regard to assessing the effects of dichoptic therapy on adults. Most studies did not consider including post-therapy follow-ups to help evaluate the effect of the therapies after some months for any possible reversals of amblyopia. Compliance with home-based treatments using dichoptic therapy has been established (using the history updates of the iPad), but more trials at home will need to be carried out using different protocols to monitor the various factors like test distance adherence and resetting the contrast of the device which are unique to home-based therapy.

Recommendations

This review showed various promising areas for future research. From the literature, it was shown that there is responsiveness to treatment for participants with severe amblyopia. In a study involving dichoptic therapy, VA, stereo-acuity and contrast sensitivity before and after treatment are the clinical characteristics that are important to report. For the classification of amblyopic type, refractive errors, eye deviation and individual training time before and after treatment should be reported. Depending on the type of amblyopia in consideration, it is recommended to carry out various visual tests for screening participants and assessing binocularity before and after treatment. It was demonstrated that there are possibilities that reduced VA was caused by suppression mechanisms. Therefore, there may be more room for reduction of suppression in more severe cases. The studies so far showed that training duration was not a limiting factor in enhancing VA; it would be vital to monitor treatment prognosis over longer periods to allow participants to reach their asymptomatic stage. It is also important to access the response of amblyopic eyes to dichoptic therapy in adults by age range. This will show if much younger adults have better improvement in visual functions compared to older adults. This can be achieved by using larger numbers of participants and having a control group in the study.

Secondly, the initial stereo-sensitivity was not an important factor in improving visual acuity; however, stereo-sensitivity was selected as a measure of binocular vision because of the use of clinical stereo-acuity in measuring binocularity.⁵³ It is therefore possible that when binocularity is measured using other types of tests, their improvement might be shown as a significant predictor of plasticity in adult amblyopia.

Finally, it is recommended that the direct visual attention, a set of cognitive operations that help in the selection of relevant and removal of irrelevant information from cluttered visual location, which is functional in the eye of anisometropic amblyopia, might play a primary role in VA and stereopsis enhancement. The elements of amblyopia

deficits can also be examined by investigating the correlation between the depth of amblyopia and the performance on visual attention functions. A positive connection would give evidence that attention harmonises suppression of the anisometropic amblyopic input.

Conclusion

Most practitioners find it challenging to manage amblyopia in adults. Dichoptic therapy affords adults with anisometropic or mixed amblyopia an opportunity to improve their binocular vision with a more satisfactory prognosis. These adult patients with residual anisometropic or mixed amblyopia may have a structurally intact visual pathway, which is functionally suppressed, leading to abnormal binocular vision. Balancing the information seen by the two eyes will enhance binocular function and re-establishment of an optimally functioning binocular vision system. Managing amblyopia in adults could result in improvement in the quality of life and help these patients to be more involved in the economically active populations of societies across the world. Practitioners now have an option to manage not only children with anisometropic or mixed amblyopia, but also adults. Further studies are required to identify the long-term benefits of dichoptic therapy on both monocular and binocular vision deficits, and more research is required to establish its success as a home and clinic-based therapy.

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