Review Article

Effectiveness of Psychophysical Visual Stimuli-Based Interventions in Amblyopia Treatment: A Systematic Review

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Running title: Visual Stimuli Interventions for Amblyopia

Abstract
Introduction: Active vision therapy, integrating perceptual learning with dichoptic or binocular environments, has shown potential effectiveness in treating amblyopia. However, uncertainties linger regarding the optimal types of stimuli and the best approaches and sequences for their presentation. This systematic review evaluates the effectiveness of psychophysical visual stimuli-based interventions, particularly perceptual learning and dichoptic training, in treating amblyopia.
Materials and Methods: A comprehensive literature search across major databases, such as PubMed and Google Scholar, yielded 26 studies involving 993 amblyopic patients. These studies

investigated various visual training methods, including perceptual learning, dichoptic stimulation, and combinations of both, with stimuli such as Gabor patches, letter optotypes, Vernier stimuli, and random-dot stereograms.
Results: The findings indicate that perceptual learning enhances visual acuity, contrast sensitivity, and stereopsis, even in adult patients, by leveraging neural plasticity. Dichoptic training, which engages both eyes simultaneously, shows promise in reducing suppression and improving binocular integration, providing a potential advantage over traditional patching therapy. Gabor patches emerged as particularly effective, stimulating the visual cortex to drive neural efficiency.
Conclusion: Vision therapy can be an effective strategy for treating amblyopia and potentially reduce the overall treatment time when used alongside patching. In addition, it is imperative to modify the stimuli to align with the distinct characteristics of the patient during both monocular and binocular training.
Keywords: Amblyopia; Orthoptics; Psychophysics; Systematic review

Introduction

Amblyopia is a developmental visual disorder characterized by reduced visual acuity in one or both eyes without any ocular pathology and not immediately correctable with lenses (1). It is commonly caused by strabismus or refractive disorders and affects about 2-4% of the general population (2, 3). Neuroimaging techniques have shown cortical abnormalities in amblyopic individuals, indicating that visual deficits, including monocular and binocular impairments, stem from anomalies in the striate and extra-striate cortex (4, 5).

Amblyopia develops during the plasticity period of the visual system, which is supposed to be the first 7-9 years of life (6). It should be mentioned that certain risk factors might increase the likelihood of developing amblyopia in childhood, including a family history of amblyopia, prematurity, low birth weight, and conditions such as Down syndrome or cerebral palsy (7). Therefore, early detection and treatment are crucial for managing amblyopia effectively and preventing long-term visual impairment.

New methods have emerged in recent years for treating amblyopia, in addition to the traditional approaches of using glasses, patching, and penalization with atropine drops or Bangerter filters (1, 7). These innovative techniques involve computer-based active vision therapy using a variety of psychophysical stimuli (8). The rationale behind these trainings is rooted in the impact of video games on neuromodulatory pathways and improving attention skills, as supported by neurophysiological studies (9, 10).

The introduction of these novel approaches has empowered clinicians to formulate innovative protocols that incorporate the following techniques: perceptual learning (11-13), dichoptic training (14-16), and binocular therapy (17-19).

The utilization of perceptual learning and/or dichoptic or binocular therapy in active vision therapy necessitates careful consideration of the stimuli employed and how they are presented. The selection of stimuli and the sequence of their presentation play a critical role in the therapy's effectiveness. Moreover, during the monocular phase, stimuli and environments are specifically chosen to facilitate visual deficit recovery, while in the binocular phase, the focus shifts towards improving interocular fusion and stereopsis (20).

Notably, the implementation of active visual therapy, which incorporates perceptual learning, dichoptic stimulation, and binocular training with anaglyph glasses, presents a captivating

avenue of research (21). This study area has the potential to enhance and refine traditional approaches to amblyopia treatment.
The present article sought to collect and review all scientific literature on the use of psychophysical visual stimuli in active vision training for amblyopia, focusing on evaluating the quality of the evidence provided.

Materials and Methods

Study design

A systematic review was conducted on different types of research studies that assessed the effects of types of stimuli on the treatment of patients with amblyopia**.**

Review protocol

The review was conducted following the recommendations of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).

Criteria for eligibility

The inclusion criteria were articles that analyze psychophysical visual stimuli in active vision training that incorporates perceptual learning, dichoptic stimulation, and binocular training for amblyopia. The present study did not restrict the timeframe or type of articles, including original research, randomized clinical trial, case series, non-randomized interventional studies, and case reports.
The studies that involved animals or primarily focused on traditional methods, such as using glasses, patching, and penalizing with atropine drops or Bangerter filters, were excluded.

Sources of information

Four electronic databases were reviewed, including Google Scholar, Web of Science, Research Gate, and PubMed.

Search strategy

In order to conduct a comprehensive literature review, an extensive search was performed using electronic databases from December 2023 to December 2024. Major databases, including Google Scholar, Web of Science, Research Gate, and PubMed, were utilized, along with two specific searching strategies (Table 1), to collect scientific literature. The Zotero reference manager platform was instrumental in organizing the gathered publications.

Table 1. Search strategies

Strategy 1: free language	
#1	Vision therapy
#2	Dichoptic
#3	Dichoptic vision therapy

#4	Perceptual learning
#5	Video games
#6	Behavioral training
#7	Computer games
#8	Virtual reality
#9	Orthoptics
#10	Binocular vision therapy
#11	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10
#12	Amblyopia
#13	Anisometropic amblyopia
#14	Strabismic amblyopia
#15	Lazy eye
#16	#12 OR #13 OR #14 OR #15
#17	Child
#18	Children
#19	Childhood
#20	Young
#21	Adults
#22	Preschool
#23	17 OR #18 OR #20 OR #21 OR #22
#24	Visual acuity
#25	VA
#26	Stereopsis

#27	Contrast sensitivity
#28	Vernier acuity
#29	Letter acuity
#30	#24 OR #25 OR #26 OR #27 OR #28 OR #29
#31	Gabor’s patches
#32	Vernier stimuli
#33	Random-dot stereograms
#34	Psychophysical stimuli
#35	Letter optotypes
#36	#31 OR #32 OR #33 OR #34 OR #35
#37	#11 AND #23 AND #30 AND #36
Strategy 2: controlled vocabulary (MeSH terms)	
#1	“Video games” [mesh]
#2	“Computer games” [mesh]
#3	“Virtual reality” [mesh]
#4	“Virtual reality exposure therapy” [mesh]
#5	“Orthoptics” [mesh]
#6	#1 OR #2 OR #3 OR #4 OR #5
#7	“Amblyopia” [mesh]
#8	“Child” [mesh]
#9	“Young adult” [mesh]
#10	“Adolescent” [mesh]
#11	“Preschool” [mesh]
#12	#8 OR #9 OR #10 OR #11 OR #11

#13	“Visual acuity” [mesh]
#14	“Depth perception” [mesh]
#15	“Contrast sensitivity” [mesh]
#16	#13 OR #14 OR #15
#17	“Psychophysics” [mesh]
#18	#6 AND #7 AND #12 AND #16 AND #17

Keywords used in search strategies of free language and controlled vocabulary includes “amblyopia”, “dichoptic vision therapy”, “perceptual learning”, “video game-based therapy”, “behavioral training”, “letter optotypes”, “”, “Gabor’s patches”, “Vernier’s stimuli”, “virtual reality”, “random-dot stereograms”, “psychophysical stimuli”, “lazy eye”, “visual acuity”, “binocular vision therapy”, “children”, “young”, “adult”.

To refine the readability and linguistic precision of certain sections of this manuscript, the Chat Generative Pre-Trained Transformer (ChatGPT) was used. This tool was employed solely for language editing purposes and was not involved in generating scientific content, conducting data analysis, or interpreting results. All outputs produced through this tool were thoroughly reviewed and edited by the author to ensure accuracy and adherence to academic standards.

Results

1. Search Results

A comprehensive search yielded an initial collection of 632 documents. Following a meticulous review of titles and abstracts, along with eliminating duplicates, 84 articles were selected for full-text evaluation. However, 58 of these articles were excluded due to non-compliance with the inclusion criteria. Consequently, 26 articles were deemed appropriate for inclusion (Figure 1).

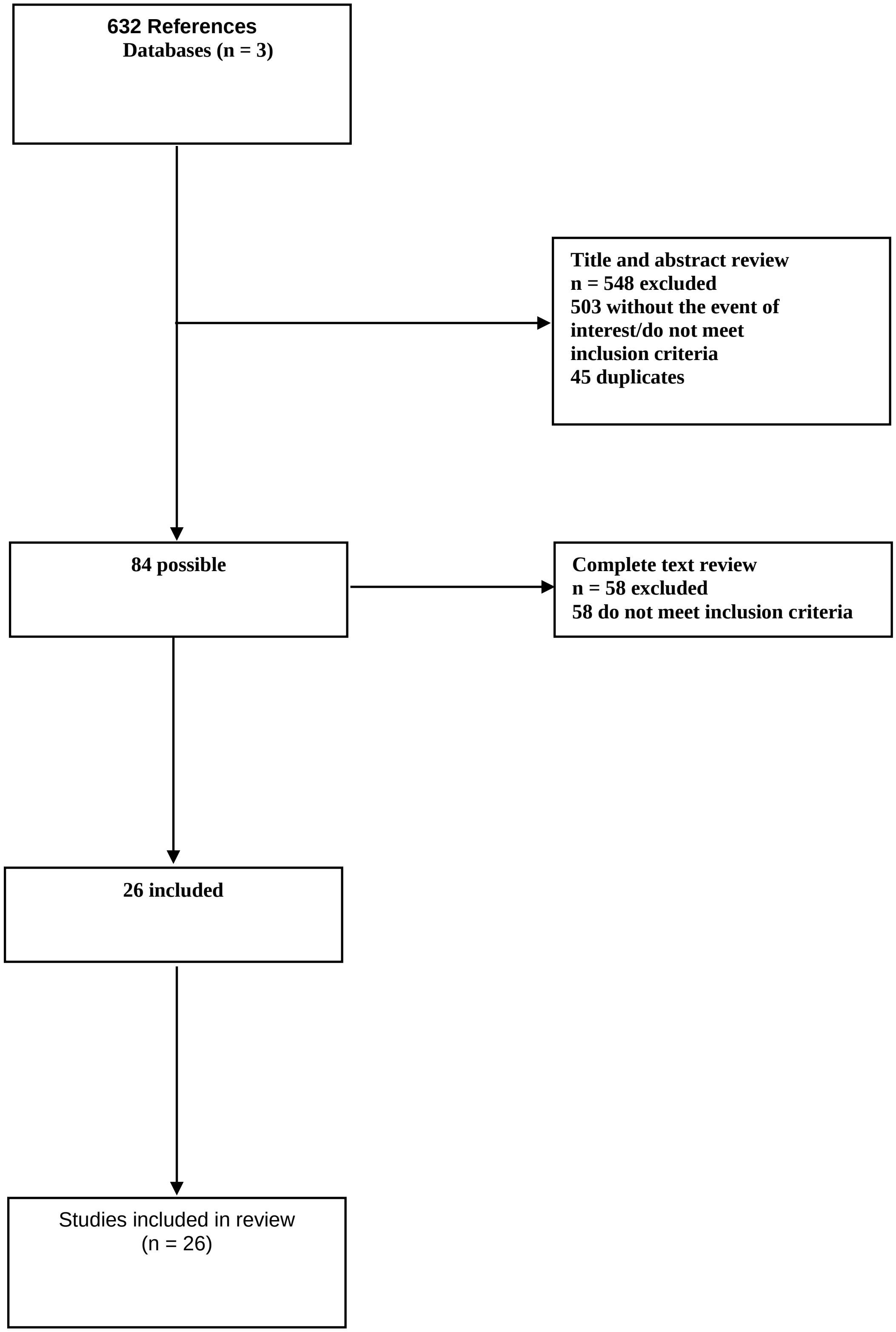

Figure 1: Flowchart showing the procedure followed during the systematic review

2. Study characteristics

Data was gathered from 993 amblyopic patients across the 26 reviewed studies. (See Table 2). The eligible studies included twenty-one cross-sectional studies (12, 22-41), two randomized control trials [42, 43], two pilot studies [44, 45], and one case-report study [46] published between 1995 and 2024.

All studies have examined the effect of visual training methods including dichoptic training and perceptual learning using different stimuli in amblyopic patients.

The articles were classified based on the type of visual stimuli used: 1) Letter Optotypes; 2) Gabor's Patches; 3) Vernier's Stimulus; 4) Random-Dot Stereograms.

Nonetheless, four specific stimuli types (Table 2) have demonstrated efficacy in clinical research and can be easily integrated into amblyopia training software, allowing for adjustments based on the patient's progress.

The intervention focused on new trends in computer-based active vision therapy, which is used to improve the visual functions of amblyopia. These were included perceptual learning training, dichoptic stimulation, and in some cases a combination of both methods.

Twenty-one studies investigated the therapeutic impacts of visual training methods such as perceptual learning (12, 27-30, 34-39, 41, 42, 45), dichoptic training (33), and perceptual learning/dichoptic training combinations (31, 32, 42) on amblyopic patients using Gabor's patch stimuli. In addition, four studies (22, 23, 26, 46) investigated the role of perceptual learning in treating amblyopia using letter optotype stimuli.

It should be noted that in three studies (40, 41, 43), random-dot stereogram stimuli were used in the treatment of amblyopia, of which two studies (41, 43) were conducted with perceptual learning method and one study (40) was conducted with perceptual learning/dichoptic training combinations.

In one study (25), the combination of Gabor's patch and letter optotype stimuli was used in the treatment of amblyopia through perceptual learning.

The remaining two studies (38, 39) in this review explored the impact of perceptual learning in the improvement of visual function in adults with amblyopia using Vernier's Stimulus.

Table 2. The main outcomes of the included studies

Study	Sample	Cause of Amblyopia	Intervention	Stimulus	Outcome
Polat et al., 2004 (24)	77	41 aniso, 36 strab	PL	Gabor's patch	two-fold improvement in CS and letter-recognition tasks
Hussain et	10	6 strab, 4	PL	Letter	reduced visual crowding in

al., 2012 (22)		mixed		optotypes	the amblyopic fovea
Chung et al., 2012 (23)	5	1 aniso, 4 strab	PL	Letter optotypes	Improvement in VA, letter CS, size of the visual span, and reduced crowding
Avram et al., 2013 (46)	5	Aniso	PL	Letter optotypes	Significant improvement of VA and CS after training
Zhang et al., 2013 (25)	341	Aniso, strab, ametropic and mixed	PL	Gabor's patch Letter optotype	Improvement in VA with PL was similar to with patching
Poltavski et al., 2024 (26)	40	Aniso	PL	Letter optotype	Improvement in BCVA with PL was similar to with patching
Li et al., 2004 (27)	7	2 Aniso, 3 strab, and 2 mixed	PL	Gabor's patch	Significant improvements in position and VA after intensive training
Li et al., 2005 (28)	5	1 Aniso, 3 strab, and 1 mixed	PL	Gabor's patch	Substantial improvement in Snellen acuity after practice
Chen et al., 2008 (44)	26	Aniso	PL	Gabor's patch	Improvement in VA by approximately three lines

					after training
Liu et al., 2011 (29)	23	16 Aniso, 4 ametropic and 3 mixed	PL	Gabor's patch	Improvement in grating acuity and Stereoacuity
Zhang et al., 2014 (30)	19	12 Aniso, 2 strab, and 5 mixed	PL	Gabor's patch	improvement of VA, CS, and stereoacuity after training
Vedamurthy et al., 2015 (31)	23	10 Aniso, 13 strab	DT and PL	Gabor's patch	improvement in suppression, Gabor resolution, VA and stereopsis
Vedamurthy et al., 2015 (32)	38	16 Aniso, 22 strab	DT and PL	Gabor's patch	Improvement in VA
Liu et al., 2018 (33)	13	9 aniso, 1 strab, 3 mixed	DT	Gabor's patch	Stereopsis improved 26.5% ± 6.9%
Shuai et al., 2019 (34)	24	12 aniso, 12 strab	PL	Gabor's patch	Significant improvements 0f VA in AA and Stereoacuity in SA
Barollo et al, 2017 (12)	10	2 Aniso, 5 strab, 1 ametropic, 1 unclassified, and 1 mixed	PL	Gabor's patch	Reduced contrast-detection thresholds
Battaglini et	6	organic bilateral	PL	Gabor's patch	Improvement in contrast

al., 2021 (45)		amblyopia			thresholds
Magdalene et al., 2022 (35)	45	39 aniso, 1 strab, 2 mixed, and 3 dep	PL	Gabor’s patch	Improvement in distance BCVA
Pérez-Benito et al., 2023 (42)	120	Aniso, strab, and mixed	DT and PL	Gabor’s patch	Improvement of VA and stereoacuity after training
He et al., 2023 (36)	49	36 Aniso, 4 strab, and 9 ametropic	PL	Gabor’s patch	Improvement of VA and CSF
Zhou et al., 2024 (37)	31	Aniso	PL	Gabor’s patch	Improvement of VA between 0.5 and 1.5 lines
Levi et al., 1996 (38)	6	Aniso	PL	Vernier’s Stimulus	Vernier acuity improved 46 ± 7%
Levi et al., 1997 (39)	11	4 Aniso, 4 strab, and 3 mixed	PL	Vernier’s Stimulus	significant and substantial improvements in Vernier acuity
Vedamurthy et al., 2016 (40)	11	2 Aniso, 4 strab, and 5 mixed	DT and PL	RDS	Reduced suppression and improved stereoacuity
Martín-González et al., 2020 (41)	16	2 aniso, 8 strab, 4 mix, 2 ametropic	PL	RDS	Significant improvement of stereopsis
Portela-Camino et al., 2018 (43)	32	2 aniso, 18 strab, 10 mixed, ametropic	PL	RDS	Stereopsis increased about 50%

Aniso: anisometropia; Strab: strabismus; Dep: derivational; DT: dichoptic training; PL: perceptual learning; VA: visual acuity; BCVA: best-corrected visual acuity; CS: contrast sensitivity; CSF: contrast sensitivity function; RDS: random-dot stereogram

Discussion

This systematic review was done to establish the efficacy of psychophysical visual stimuli, namely perceptual learning and dichoptic training techniques, in managing amblyopia. The findings underline the effectiveness of specific stimuli, such as Gabor patches, letter optotypes, Vernier's stimulus, and random-dot stereograms in improving visual function across types and severities of amblyopia.

Studies reviewed here provide strong evidence that perceptual learning and dichoptic training may be a promising therapeutic intervention with wide-ranging implications for improving visual acuity, contrast sensitivity, and stereopsis, reducing crowding effects.

1. Perceptual learning in amblyopia treatment

Indeed, perceptual learning has emerged as a valuable strategy for improving visual function in individuals with amblyopia. Evidence is that intensive training may result in meaningful enhancements in visual acuity and other visual tasks, even among adults with long-standing amblyopia (27, 44). Several reports (28, 29) indicated that perceptual learning training with Gabor patches and letter optotypes effectively improved visual acuity and contrast sensitivity in children and adults. Such improvements suggest the capability of perceptual learning in inducing plasticity in the visual system and hence, it is potential for therapy well beyond the critical period of visual development.

The training focused on improving peripheral visual tasks also showed promising results. Enhancing letter recognition performance through training at 10° eccentricity in the visual field revealed significant improvements (47), indicating that perceptual learning interventions are versatile and can address both central and peripheral visual deficits.

Besides, perceptual learning using letter optotypes has been considered effective, according to several studies (23, 26, 46), for improving visual acuity and reducing crowding effects in pediatric and adult amblyopes. According to the studies, letter optotype-based tasks are practical and can be easily delivered through various formats like video games or software platforms. This would suggest that, clinically, improving visual acuity, especially in anisometropic amblyopia, might offer an additional benefit on daily visual functions, at least for reading and object recognition, both important activities in everyday life.

2. Crowding and contrast sensitivity

One of the major objections to amblyopic defectives is the crowding effect, wherein object recognition is impaired in cluttered visual backgrounds. The studies reviewed here thus demonstrate that perceptual learning regimens targeting the crowding effects reduce this impairment (23, 24). These studies did measure improvements in letter identification and acuity, which may suggest that perceptual learning, as opposed to merely reducing the crowding effect, might improve performance in practical visual tasks like reading.

Moreover, contrast sensitivity-a very frequently deficient aspect of visual function in amblyopia-always showed improvement after perceptual learning interventions. Gabor patch training protocols resulted in significantly reduced and ameliorated thresholds in detecting contrasts (12, 24), showing the capability of such stimuli to enhance fine visual discrimination. Such findings highlight the potentiality of perceptual learning in restoring higher-order visual processing-a very significant constituent of visual function in daily life.

3. The role of dichoptic training

Of late, dichoptic training has appeared as especially effective in the binocular deficits of amblyopia, particularly targeting suppression and enhancing stereopsis. In contrast to monocular patching treatment, which reinforces a weaker eye at the cost of an advantage to the leading eye, dichoptic training embarks on activating both eyes to facilitate binocular integration (31). This technique uses separately presented stimuli to each eye in such a way as to limit suppression and enhance the visual function of the amblyopic eye without affecting impairment in the functioning of the dominant eye.

Several studies (31, 34) have demonstrated that dichoptic training interventions successfully reduce suppression and improve visual acuity, contrast sensitivity, and stereopsis. Specifically, some video games are specially designed to incorporate dichoptic stimuli and are particularly effective and enjoyable, interactive, patient-friendly modes of therapy. These games utilize Gabor patches or similar stimuli to excite both eyes together, which helps elicit binocular cooperation and reduces imbalance between the eyes (31).

Indeed, the effects of dichoptic training extend well over and above any linear improvement in visual acuity. Several studies (32, 42) using customized dichoptic video games have reported improved stereopsis, reduced suppression, and increased contrast sensitivity in children and adults with amblyopia. Forms of this kind of training allow an integration of visual information across both eyes in patients, which results in improved depth perception and binocular visual function.

The reviewed studies (32, 48) also demonstrated that dichoptic training regimens could supplement or even surpass traditional therapies in certain aspects. The video game-based dichoptic treatments were more time-effective, amplifying best-corrected visual acuity compared to traditional patching therapy. These findings support the influence of dichoptic training as a strong alternative to monocular treatments by offering a more holistic approach: improving monocular and binocular visual functions.

4. Effectiveness of Gabor patches

Gabor patches have been among the most effective stimuli that have repeatedly evoked perceptual learning in amblyopes. Their spatial properties resemble the receptive field characteristics of neurons in the visual cortex and, thus, are particularly effective at driving neural plasticity (49). Indeed, studies (25, 27) across different patient groups documented that training with Gabor patches significantly improved visual acuity, contrast sensitivity, and stereoacuity. This suggests that Gabor patches are well suited for optimizing neuronal efficiency by increasing contrast sensitivity and reducing the signal-to-noise ratio in the primary visual cortex.

Additionally, dichoptic training with Gabor patches has proved effective in amblyopia treatment. Thus, Gabor patches with dichoptic presentation have the added advantage of allowing both eyes to be selectively stimulated to promote binocular integration and reduce suppression (31, 34). This technique not only improves monocular visual functions such as visual acuity and contrast sensitivity, but it also promotes binocular vision in problems of stereopsis and depth perception.

5. Vernier acuity and stereopsis

Perceptual learning tasks focusing on Vernier acuity also effectively improved visual function in amblyopia. Significant gains in Vernier acuity were observed following extensive training (50, 51), suggesting that perceptual learning can enhance fine visual tasks that require precise alignment or discrimination. Improvements in Vernier acuity were particularly evident in tasks involving line tilt detection and stereoacuity, both critical aspects of visual hyperacuity (52).
Notably, Levi and Polat (38) demonstrated that neural plasticity in adults with amblyopia could be leveraged to enhance Vernier acuity through perceptual learning, revealing the potential for significant gains in fine spatial discrimination. This improvement is critical, reflecting enhanced visual processing capabilities beyond basic acuity measures.
Further supporting these findings, Levi, Polat, and Hu (39) showed that practice could substantially improve Vernier acuity in adults with amblyopia. Their study highlighted that adult amblyopes could achieve better alignment detection with consistent practice, suggesting that perceptual learning can lead to meaningful enhancements in high-resolution visual tasks. This evidence underscores the potential for perceptual learning to improve complex visual functions, which are crucial for activities requiring high spatial resolution
Stereopsis, which is often compromised in individuals with amblyopia, showed substantial improvement following perceptual learning interventions. Studies (52, 55) involving training programs focused on stereoacuity demonstrated significant gains in-depth perception, even in adult patients previously considered stereo-blind. These findings are particularly encouraging as they challenge the traditional view that stereopsis cannot be recovered after the critical period of visual development. Perceptual learning interventions have proven to be effective in restoring binocular vision and depth perception, even in patients with severe amblyopia.

6. Comparison with conventional therapies

Perceptual learning, particularly through dichoptic training and Gabor patch interventions, offers a targeted and effective alternative to conventional therapies for amblyopia. Traditional methods, such as patching and refractive correction, primarily aim to improve visual acuity in the amblyopic eye, often leading to reduced binocular vision (27). In contrast, perceptual learning addresses a broader range of visual deficits, including contrast sensitivity, crowding, and stereopsis, making it a more comprehensive treatment approach (23).
Dichoptic training, in particular, provides an advantage over monocular therapies by engaging both eyes simultaneously, promoting binocular integration, and reducing suppression (31). This dual-eye approach enhances overall visual function and can improve stereopsis and depth perception more sustainably. The versatility of perceptual learning, especially when combined with traditional treatments, allows for more individualized therapy regimens that cater to each patient's specific needs (48).

7. Effects Based on Depth of Amblyopia, Patient Age, and Binocular Vision Status

The responses to perceptual learning and dichoptic training are, to some extent, moderated by the depth of amblyopia and age of the patients. In patients with mild to moderate amblyopia, perceptual learning with Gabor patches and letter optotypes has significantly improved contrast sensitivity and visual acuity (27, 28, 29). In severe amblyopia, as with many things in this condition, the response is much more multifaceted and requires longer training times to produce the same results (31, 34).
The patient's age is also another vitally important factor in the treatment response. Younger patients, particularly children, seem to benefit at an earlier stage from the intervention to retain

improvement over a longer period in visual performance (23, 26). Still, there is some evidence that even older adults are capable of experiencing changes due to neuroplastic changes from perceptual learning capable of impacting vision for the better (27, 44). For example, training with Gabor patches was shown to benefit contrast sensitivity and binocular vision in patients with amblyopia (25, 27).

Furthermore, the status of binocular vision significantly influences treatment outcomes. Dichoptic training has been shown to reduce suppression and enhance stereopsis (depth perception). Video game-based dichoptic treatments, in particular, have demonstrated the potential to improve monocular visual functions and binocular cooperation (31, 32, 42). These findings highlight that perceptual learning and dichoptic training-based therapies can offer a comprehensive approach to improving visual function across different amblyopia profiles.

8. Limitations and future research

Despite the promising findings, several limitations need to be addressed. Many of the studies included in this review had small sample sizes, limiting the generalizability of the results. Furthermore, the variability in training protocols and outcome measures across studies complicates the ability to draw definitive conclusions about the most effective intervention strategies. Additionally, long-term follow-up data are lacking in many cases, making it difficult to determine the durability of the visual improvements achieved through perceptual learning (28, 34).

Future research should focus on large-scale randomized controlled trials (RCTs) with standardized training protocols and outcome measures. This would help establish a more robust evidence base for the use of perceptual learning in amblyopia treatment. Additionally, further investigation is needed into the long-term sustainability of the improvements achieved through these interventions (32). Longitudinal studies that track patients' progress over time will be crucial in determining whether perceptual learning can prevent the regression of visual function after treatment (12).

Finally, exploring the combination of perceptual learning with conventional therapies could yield even greater treatment efficacy. Combining therapies may offer a more comprehensive approach to amblyopia treatment by addressing both suppression and visual deficits. Investigating the synergistic effects of such combined interventions could lead to more effective and personalized treatment regimens for amblyopia (42).

Conclusion

There is evidence from this systematic review that psychophysical visual stimuli may be effective treatments for amblyopia, especially through perceptual learning. The treatments consistently improved visual acuity, contrast sensitivity, crowding, and stereopsis across diverse populations. Dichoptic training, in particular, offers a powerful alternative to traditional therapies through binocular integration and reduced suppression. With the evolving research in the field, perceptual learning-based interventions may form an essential part of amblyopia management and thus provide patients personalized, effective treatment options.

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References;

1. Von Noorden G, Campos E. Binocular Vision and Ocular Motility. 6 eds. St. Louis, Missouri: Mosby, Inc; 2002.
2. Evans BJW. Pickwell's Binocular Vision Anomalies: Investigation and Treatment, 4th ed. Oxford: Butterworth-Heinemann; 2002.
3. DeSantis D. Amblyopia. Pediatric Clinics of North America. 2014; 61(3):505-18.
4. Anderson SJ, Swettenham JB. Neuroimaging in human amblyopia. Strabismus. 2006; 14(1):21-35.
5. Körtvélyes J, Bankó É, Andics A, Rudas G, Németh J, Hermann P, Vidnyánszky Z. Visual cortical responses to the input from the amblyopic eye are suppressed during binocular viewing. Acta Biologica Hungarica. 2012; 63(Supplement-1):65-79.
6. Özdek, Ş., Berrocal, A., Spandau, U. Pediatric Vitreoretinal Surgery. 1st ed. Springer; 2023
7. Moore B D. Eye Care for Infants and Young Children. Boston; Butterworth, 1998.
8. Kraus CL, Culican SM. New advances in amblyopia therapy I: binocular therapies and pharmacologic augmentation. British Journal of Ophthalmology. 2018; 102(11):1492-6.
9. Coco-Martin MB, Valenzuela PL, Maldonado-López MJ, Santos-Lozano A, Molina-Martín A, Piñero DP. Potential of video games for the promotion of neuroadaptation to multifocal intraocular lenses: a narrative review. International Journal of Ophthalmology. 2019; 12(11):1782.
10. Dye, M.W.G., Green, C.S., Bavelier, D. The development of attention skills in action video game players. Neuropsychologia. 2009; 47(8-9):1780-9.
11. Levi DM, Li RW. Perceptual learning as a potential treatment for amblyopia: a mini-review. Vision research. 2009; 49(21):2535-49.
12. Barollo M, Contemori G, Battaglini L, Pavan A, Casco C. Perceptual learning improves contrast sensitivity, visual acuity, and foveal crowding in amblyopia. Restorative neurology and neuroscience. 2017; 35(5):483-96.

13. Deshpande PG, Bhalchandra PC, Nalgirkar AR, Tathe SR. Improvement of visual acuity in residual meridional amblyopia by astigmatic axis video games. Indian Journal of Ophthalmology. 2018; 66(8):1156-60.
14. Li J, Thompson B, Deng D, Chan LY, Yu M, Hess RF. Dichoptic training enables the adult amblyopic brain to learn. Current Biology. 2013; 23(8): R308-9.
15. Liu XY, Zhang YW, Gao F, Chen F, Zhang JY. Dichoptic perceptual training in children with amblyopia with or without patching history. Investigative ophthalmology & visual science. 2021; 62(6):4.
16. Iwata Y, Handa T, Ishikawa H, Goseki T, Shoji N. Comparison between Amblyopia Treatment with Glasses Only and Combination of Glasses and Open-Type Binocular “Occlu-Pad” Device. BioMed research international. 2018; 2018(1):2459696.
17. Birch EE, Li SL, Jost RM, Morale SE, De La Cruz A, Stager Jr D, Dao L, Stager Sr DR. Binocular iPad treatment for amblyopia in preschool children. Journal of American Association for Pediatric Ophthalmology and Strabismus. 2015; 19(1):6-11.
18. Li SL, Jost RM, Morale SE, Stager DR, Dao L, Stager D, Birch EE. A binocular iPad treatment for amblyopic children. Eye. 2014; 28(10):1246-53.
19. Holmes JM, Manh VM, Lazar EL, Beck RW, Birch EE, Kraker RT, Crouch ER, Erzurum SA, Khuddus N, Summers AI, Wallace DK. Effect of a binocular iPad game vs part-time patching in children aged 5 to 12 years with amblyopia: a randomized clinical trial. JAMA ophthalmology. 2016; 134(12):1391-400.
20. 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. Journal of clinical medicine. 2020; 9(12):3985.
21. Foss AJ. Use of video games for the treatment of amblyopia. Current opinion in ophthalmology. 2017; 28(3):276-81.
22. Hussain Z, Webb BS, Astle AT, McGraw PV. Perceptual learning reduces crowding in amblyopia and in the normal periphery. Journal of Neuroscience. 2012; 32(2):474-80.
23. Chung ST, Li RW, Levi DM. Learning to identify near-acuity letters, either with or without flankers, results in improved letter size and spacing limits in adults with amblyopia. Plos one. 2012; 7(4): e35829.
24. Polat U, Ma-Naim T, Belkin M, Sagi D. Improving vision in adult amblyopia by perceptual learning. Proceedings of the National Academy of Sciences. 2004; 101(17):6692-7.
25. Zhang W, Yang X, Liao M, Zhang N, Liu L. Internet-based perceptual learning in treating amblyopia. European journal of ophthalmology. 2013; 23(4):539-45.
26. Poltavski D, Adams RJ, Biberdorf D, Patrie JT. Effectiveness of a novel video game platform in the treatment of pediatric amblyopia. Journal of Pediatric Ophthalmology & Strabismus. 2024; 61(1):20-9.

27. Li RW, Levi DM. Characterizing the mechanisms of improvement for position discrimination in adult amblyopia. Journal of vision. 2004; 4(6):7.
28. Li RW, Young KG, Hoenig P, Levi DM. Perceptual learning improves visual performance in juvenile amblyopia. Investigative ophthalmology & visual science. 2005; 46(9):3161-8.
29. Liu XY, Zhang T, Jia YL, Wang NL, Yu C. The therapeutic impact of perceptual learning on juvenile amblyopia with or without previous patching treatment. Investigative ophthalmology & visual science. 2011; 52(3):1531-8.
30. Zhang JY, Cong LJ, Klein SA, Levi DM, Yu C. Perceptual learning improves adult amblyopic vision through rule-based cognitive compensation. Investigative ophthalmology & visual science. 2014; 55(4):2020-30.
31. Vedamurthy I, Nahum M, Bavelier D, Levi DM. Mechanisms of recovery of visual function in adult amblyopia through a tailored action video game. Scientific reports. 2015; 5(1):8482.
32. 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 research. 2015; 114:173-87.
33. Liu XY, Zhang JY. Dichoptic training in adults with amblyopia: Additional stereoacuity gains over monocular training. Vision Research. 2018; 152:84-90.
34. Shuai L, Leilei Z, Wen W, Shu W, Gangsheng L, Yinglong L, Guoke Y, Xinrong C, Hong L, Rongfeng L. Binocular treatment in adult amblyopia is based on parvocellular or magnocellular pathway. European Journal of Ophthalmology. 2020; 30(4):658-67.
35. Magdalene D, Dutta P, Opt M, Deshmukh S, Ophthal DN, Borah CJ, Nath RP, Opt B. Neural Vision Perceptual Learning as an Effective Treatment of amblyopia. Vision Development & Rehabilitation. 2022; 8(4):260-9.
36. He Y, Feng L, Zhou Y, Zhuang Y, Xu Z, Yao Y, Chen X, Jiang R, Yuan J, Ye Q, Wen Y. Characteristics and predictive factors of visual function improvements after monocular perceptual learning in amblyopia. Heliyon. 2023; 9(6).
37. Zhou Y, He Y, Feng L, Jia Y, Ye Q, Xu Z, Zhuang Y, Yao Y, Jiang R, Chen X, Pang Y. Perceptual learning based on the lateral masking paradigm in anisometropic amblyopia with or without a patching history. Translational vision science & technology. 2024; 13(1):16-.
38. Levi DM, Polat U. Neural plasticity in adults with amblyopia. Proceedings of the National Academy of Sciences. 1996; 93(13):6830-4.
39. Levi DM, Polat U, Hu YS. Improvement in Vernier acuity in adults with amblyopia. Practice makes better. Investigative ophthalmology & visual science. 1997; 38(8):1493-510.
40. Vedamurthy I, Knill DC, Huang SJ, Yung A, Ding J, Kwon OS, Bavelier D, Levi DM. Recovering stereo vision by squashing virtual bugs in a virtual reality environment.

Philosophical Transactions of the Royal Society B: Biological Sciences. 2016; 371(1697):20150264.

41. Martín-González S, Portela-Camin J, Ruiz-Alcocer J, Illarramendi-Mendicute I, Garrido-Mercado R. Stereoacuity improvement using random-dot video games. Journal of Visualized Experiments. 2020; 155: e60236.
42. Pérez-Benito M, Calderón-González T, Álvarez-Martín E, Martín-González S, Portela-Camino JA. Study protocol for a randomized controlled trial using VISIONARY, a dichoptic Gabor patch video game, to improve visual function in children with amblyopia. Res Sq 3772007 [Preprint]. 2023.
43. Portela-Camino JA, Martín-González S, Ruiz-Alcocer J, Illarramendi-Mendicute I, Garrido-Mercado R. A random dot computer video game improves stereopsis. Optometry and Vision Science. 2018; 95(6):523-35.
44. 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 and Physiological Optics. 2008; 28(5):422-8.
45. Battaglini L, Oletto CM, Contemori G, Barollo M, Ciavarelli A, Casco C. Perceptual learning improves visual functions in patients with albinistic bilateral amblyopia: a pilot study. Restor Neurol Neurosci. 2021; 39:45–59
46. Avram E, Stănilă A. Treating anisometric amblyopia with HTS Amblyopia iNet Software--preliminary results. Oftalmologia (Bucharest, Romania: 1990). 2013; 57(2):32
47. Chung STL, Legge GE, Cheung SH. Letter-recognition and reading speed in peripheral vision benefit from perceptual learning. Vision Research. 2004; 44:695–709.
48. Li RW, Provost A, Levi DM. Extended perceptual learning results in substantial recovery of positional acuity and visual acuity in juvenile amblyopia. Investigative ophthalmology & visual science. 2007; 48(11):5046-51.
49. Durrie D, McMinn PS. Computer-based primary visual cortex training for treatment of low myopia and early presbyopia. Transactions of the American Ophthalmological Society. 2007; 105:132.
50. Saarinen J, Levi DM. Perceptual learning in vernier acuity: what is learned? Vision research. 1995; 35(4):519-27.
51. Westheimer G, Hauske G. Temporal and spatial interference with vernier acuity. Vision research. 1975; 15(10):1137-41.
52. Li RW, Levi DM. Slow Perceptual Learning of Vernier Acuity in Adult Amblyopia: An Intensive Amblyopia Treatment Study. Investigative Ophthalmology & Visual Science. 2007; 48(13):4889.
53. Astle AT, McGraw PV, Webb BS. Recovery of stereo acuity in adults with amblyopia. Case Reports. 2011; 2011: bcr0720103143.
54. Ding J, Levi DM. Recovery of stereopsis through perceptual learning in human adults with abnormal binocular vision. Proceedings of the National Academy of Sciences. 2011; 108(37): E733-41.

55. Li RW, Ngo C, Nguyen J, Lam J, Nia B, Ren D, Levi D. Playing video game improves visual acuity and visual attention in adult amblyopia-A potentially useful tool for amblyopia treatment. Investigative Ophthalmology & Visual Science. 2008; 49(13):2832.