Review Article

A Brief of Review of Amblyopia and its Management

Seyed Saber Sahihalnasab [*1], MS; Nader Nassiri [2], MD; Alireza Mohamadi [1], PhD

1. Faculty of Rehabilitation, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2. Imam Hossein Medical Center, Shahid Beheshti University of Medical Sciences

***Corresponding Author:** Seyed Saber Sahihalnasab
E-mail: saber.sahih@yahoo.com

Abstract

Amblyopia, or “lazy eye,” is the leading cause of unilateral vision impairment in children worldwide, with a prevalence of 3.7 %. This condition results from early visual deprivation or improper light focus in one eye, leading to an imbalance in visual input to the brain’s visual cortex. Consequently, vision in the affected eye declines, disrupting binocular coordination. When one eye sends unclear signals, the brain suppresses its input. Beyond visual coordination, amblyopia can impact tasks such as hand-eye coordination, reading, and self-perception. Various treatments have been developed for amblyopia in both children and adults. However, both traditional and modern treatments have limitations regarding effectiveness and patient comfort, affecting individuals and their families. A more practical approach may involve simultaneous stimulation of both eyes to enhance vision in the weaker eye, reduce suppression, and strengthen binocular vision. This review aims to provide a concise, evidence-based overview of amblyopia, covering its pathogenesis, classification, diagnosis, and treatment. By highlighting sensory adaptations and advancements in therapy, we emphasize the importance of early intervention and emerging neuroplasticity-based treatments to improve clinical outcomes.

Keywords: Amblyopia; Binocular Vision; Eccentric Fixation.

Article Notes: Article Notes: Received: May. 09, 2024; Received in revised form: Jun. 03, 2024; Accepted: Jun. 23, 2024; Available Online Sep.22, 2024.

How to cite this article: Sahihalnasab SS; Nassiri N, Mohamadi A. A Brief of Review of Amblyopia and its Management. Journal of Ophthalmic and Optometric Sciences . 2024;8(4):30-37.

Introduction

Amblyopia is a form of vision loss not attributed to structural eye abnormalities and occurs when there is a significant di fference in focusing ability between the two eyes [1]. It is diagnosed when visual acuity is less than 6/12 without any clinical cause or when there is a difference of more than two lines in visual acuity between the eyes [2]. Adults with unilateral amblyopia are three times more likely, and children 17 times more likely, to lose vision in the unaffected eye. The condition is more prevalent among premature infants and families with a history of amblyopia [3] (Table 1). If a newborn experiences light deprivation, blurriness, or improper focus during the critical period of early infancy, amblyopia can develop. This critical period peaks from birth to two years of age and gradually declines until around eight years old [4]. This review aims to provide a concise, evidence-based overview of amblyopia, covering its pathogenesis, classification, diagnosis, and treatment. By highlighting sensory adaptations and advancements in therapy, we emphasize the importance of early intervention and emerging neuroplasticity-based treatments to improve clinical outcomes.

Table 1: Amblyopia risk factors

Family history of amblyopia
Family history of squint
Pediatric cataract and glaucoma
Premature birth
Delayed neurological and visual idiopathic maturation
Socioeconomic
Factors Refractive errors, and visual deprivation in early childhood

Pathogenesis

During infancy, the cortical circuitry remains immature, and both neural pathways and the visual cortex are highly adaptable to change. For proper development, visual input from both eyes must be balanced [5]. Extensive research on amblyogenic conditions (Table 2), where visual experience is unequal, has demonstrated structural changes in both neural pathways and the cortex. These changes include thinning of ganglion cells in the affected pathway and hypertrophy of the lateral geniculate nucleus (LGN) [6-8]. Consequently, the speed of neural transmission in the affected eye is reduced, with evident morphological and functional alterations observed at the retinal level and beyond [9,10].

Ganglion cells in the retina are classified into two main types: parvocellular (P cells) and magnocellular (M cells). P cells are primarily located in the foveal and parafoveal regions, whereas M cells are distributed in peripheral retinal areas. These ganglion cells are highly sensitive to motion direction, responding when an image moves in one direction but not the other. P cells play a critical role in

Table 2: Etiology of amblyopia

1	Strabismus (50 %)
2	Anisometropia (17 %)
3	Strabismus + anisometropia (30 %)
4	Ametropia (3 %)
5	Sensory deprivation (3 %)
6	Other (3 %)

fine visual acuity, high-resolution stereopsis, and color vision, while M cells contribute to stereopsis and motion detection [11]. The cortical representation of P cells is significantly larger in sensory processing areas than that of M cells [12]. Studies have shown that amblyopic changes predominantly affect the parvocellular (P) pathway [13].

Symptoms and Types of Amblyopia

Although reduced visual acuity is the primary symptom of amblyopia, other manifestations include asymmetric eye movements, impaired contrast sensitivity, disrupted binocular vision, and deficits in hand-eye coordination [14] (Table 3).

Recent evidence suggests that the perceptual impact of amblyopia extends beyond vision, affecting multisensory processing. Abnormalities have been observed in audiovisual speech perception, spatial auditory and visual localization, and temporal judgment tasks [15-17].

Classification of Amblyopia

Amblyopia can be classified based on various criteria, including the affected eye's orientation, severity, and underlying cause (Table 4). The most common types of amblyopia are strabismic and mixed (combined mechanism) amblyopia.

Diagnosis

Amblyopia develops and progresses early in childhood, making timely screening essential before the critical period ends. Since infants and young children have limited cooperation, non-verbal and gross motor tests are necessary. A comprehensive evaluation should include visual acuity assessment, refractive status, binocular vision testing, and ocular pathology screening.

For young children, visual acuity tests such as Forced Preferential Looking (FPL), Sheridan Gardiner, and Teller Acuity Cards are recommended. In non-cooperative or suspected cases, Visual Evoked Potential

Table 3: Signs and symptoms of amblyopia

signs	symptoms
Astigmatism difference more than 1.5 D	Frequent squint, rubbing of the eye, and closing one eye
Hyperopia difference more than 1 D	Turning the head to one side
Myopia difference more than 3 D	Reading difficulties: skipping words, misreading, and substituting words. Stressful reading and fatigue
Astigmatism more than 2 D in both eyes	Messy handwriting is because of poor binocular coordination
Myopia more than 5 D in both eyes	Sport performance difficulties due to faulty depth perception, frequent tripling, and falling bumping
Hyperopia more than 2 D in both eyes	Reduced fine motor skills
Media opacity	Attention difficulties due to reduced focus
	Defective vision without any organic ocular morbidity

Table 4: Classification of definitions

Definition	Category
Based on orientation	Monucular or Binocular
Based on underlying cause	**1. Refractive Amblyopia** **Isometropic Amblyopia:** Occurs when high but equal refractive errors in both eyes lead to blurred vision and abnormal visual development. **Anisometropic Amblyopia:** Results from a significant refractive difference between the two eyes, causing the brain to favor the clearer image from one eye while suppressing the other. **2. Strabismic Amblyopia** Develops when misalignment of the eyes (strabismus) causes the brain to ignore input from the deviating eye to avoid double vision. **3. Deprivation (Stimulus-Deprivation) Amblyopia** Caused by obstruction of visual input in early childhood, such as congenital cataracts, ptosis, or corneal opacities, leading to insufficient stimulation of the visual cortex. **4. Mixed (Combined-Mechanism) Amblyopia** A combination of refractive and strabismic amblyopia, often seen in children with both significant refractive errors and ocular misalignment. **5. Occlusion (Reverse) Amblyopia** Occurs when excessive or improper patching of the dominant eye in amblyopia treatment suppresses its visual function, leading to vision loss in the previously unaffected eye.
Based on Severity	Mild: 6/9 to 6/12 Moderate: 6/12 to 6/36 Severe: Worse than 6/36
Based on ability to treat	Treatable Non-treatable

(VEP) testing is advised [18]. Binocular vision assessment involves Hirschberg, Brückner, and Cover tests. Red Reflex Testing helps evaluate media clarity in young children, while a detailed slit-lamp examination is necessary to rule out conditions such as cataracts, ptosis, or large eyelid cysts [19].

Refractive evaluation can be performed using photo-screening and retinoscopy to determine refractive errors in children [20]. One of the

Table 5: Treatment methods for amblyopia

Treatment	Procedure
Optical correction	Refractive error estimation under cycloplegia; Optical correction depends on binocular vision; Hyperopia is fully corrected in cases of esotropia.
Occlusion	Therapy using an eye patch to cover the non-amblyopic eye for a few hours daily (according to the guidelines); children under six years old should be monitored carefully for occlusion amblyopia.
Penalization	Cycloplegia of the non-amblyopic or amblyopic eye can be considered for children who do not show improvement with glasses alone or have poor compliance with patching due to various factors, including the presence of latent nystagmus or the need for maintenance therapy.
Pharmaceutical treatment	Various medications, such as Levodopa-Carbidopa and Citicoline, have been proposed and are currently under evaluation.
Refractive surgery	In children with special social and psychological conditions, as well as those with high myopic or hypermetropic anisometropia.
Alternative therapies	Includes vision therapy, perceptual learning, dichoptic therapy, acupuncture, magnetic brain stimulation, monocular video game play, Liquid Crystal Display (LCD) eyeglasses, and perceptual learning.

major diagnostic challenges in amblyopia is the evaluation of very young children and the detection of subtle amblyogenic factors. In some adults, amblyogenic factors may have resolved over time, yet amblyopia persists. In such cases, a complete anterior and posterior segment examination is required to rule out other underlying pathological conditions.

Sensory Adaptations in Amblyopia

The most common causes of amblyopia are strabismus, anisometropia, or a combination of both. Amblyopia is primarily characterized by ocular misalignment and impaired binocular vision.

Suppression is an unconscious neural adaptation in which the brain ignores input from the affected eye to eliminate visual disturbances such as confusion, aniseikonia, and diplopia. Studies suggest that deeper suppression is correlated with more severe amblyopia [21]. Children with prolonged amblyopia may develop alternative adaptive mechanisms instead of suppression, including anomalous retinal correspondence (ARC) and eccentric fixation (EF) [22].

Anomalous retinal correspondence develops to preserve some degree of binocular vision. In this condition, the brain incorrectly pairs non-corresponding retinal points between the two eyes, a phenomenon attributed to cortical-level adaptation [23]. ARC is more common in children due to their higher neuroplasticity, particularly in cases of early-onset strabismus before the age of three [24]. In some cases, ARC is clinically evident, while in others, it fluctuates depending on conditions. The depth of ARC is determined by the strength of the anomalous retinal point. Long-standing, stable strabismus is associated with deeper ARC [25].

ARC is diagnosed by comparing objective and subjective measurements using Bagolini lenses, Worth 4-dot testing, afterimage testing, red lens testing, and synoptophore examination for deeper ARC cases [26]. ARC may occur alone or alongside eccentric fixation, making treatment more challenging and less predictable. For stable binocular vision recovery, treatments include neutral prism prescription, frequent prism adjustments, macular massage, and flashing light stimulation in an amblyoscope [27]. Eccentric fixation is another adaptation in which a non-foveal retinal point assumes fixation, even under monocular conditions. Research on EF remains limited, and its exact cause is still unclear. However, studies suggest that EF occurs in cases of long-standing amblyopia, strabismus, and central vision deficits, making treatment significantly more difficult [19]. EF is diagnosed using visuoscopy and microperimetry [28]. Visual acuity declines more severely as the distance from the fovea increases. Patients with EF often exhibit greater ocular motor dysfunctions.

Treatment for EF includes red lens therapy with or without reverse patching, flashing light therapy in the amblyoscope, pleoptic therapy, and biofeedback training [27, 29].

Treatment

Research suggests that early treatment leads to faster and more effective results, though visual acuity improvements can still occur in older children and adolescents [30]. The primary goal of both traditional and modern treatments is to improve vision in the amblyopic eye and achieve stable binocular function.

Treatment should be individualized based on age, visual acuity, type of amblyopia, previous treatment response, and the child's physical, social, and psychological status [31]. Although glasses and patching remain the gold standard for treatment, no study has directly compared different therapeutic approaches.

In cases of ARC or EF, the depth of adaptation and feasibility of treatment should be assessed before initiating therapy [32].

Conclusion

Amblyopia is a common condition that affects the development of the visual pathway, leading to reduced vision and functional visual impairments, particularly in children and individuals under 40 years old. It is often caused by prolonged abnormal retinal stimulation. Early screening can aid in timely diagnosis, and prompt treatment may help reduce the prevalence of amblyopia.

Although amblyopia treatment is generally successful, the presence of adaptive mechanisms such as ARC and EF can make management more challenging. While traditional methods, such as part-time patching, are still widely used, modern approaches focus on enhancing vision in the amblyopic eye through techniques that stimulate both eyes simultaneously.

Authors ORCIDs

Seyed Saber Sahihalnasab:
https://orcid.org/0000-0001-5068-7371

References

1. Rajavi Z, Sabbaghi H, Baghini AS, Yaseri M, Moein H, Akbarian S, et al. Prevalence of Amblyopia and Refractive Errors Among Primary School Children. J Ophthalmic Vis Res. 2015;10(4):408-16.
2. McKee SP, Levi DM, Movshon JA. The pattern of visual deficits in amblyopia. J Vis. 2003;3(5):380-405.
3. Gupta SB, Kashiv Y, Gaikwad H. Treatment of amblyopia: an update. MGM Journal of Medical Sciences. 2023;10(4):789-93.
4. Hensch TK, Quinlan EM. Critical periods in amblyopia. Vis Neurosci. 2018;35:E014.
5. Espinosa JS, Stryker MP. Development and plasticity of the primary visual cortex. Neuron. 2012;75(2):230-49.
6. Al-Haddad C, Bou Ghannam A, El Moussawi Z, Rachid E, Ismail K, Atallah M, et al. Multifocal electroretinography in amblyopia. Graefes Arch Clin Exp Ophthalmol. 2020;258(3):683-91.
7. Fogt N, Jones R. The effect of forced vergence on retinal correspondence. Vision Res. 1998;38(18):2711-9.
8. Tremain KE, Ikeda H. Relationship between amblyopia, LGN cell "shrinkage" and cortical ocular dominance in cats. Exp Brain Res. 1982;45(1-2):243-52.
9. Dahal M, Dahal HN, Gautam P, Shrestha JB, Khanal S. Pattern visual evoked potential and foveal sensitivity in amblyopia. Doc Ophthalmol. 2023;147(2):109-19.
10. Wan J, Zhang Z, Tian Y. Examination of Macular Retina and Choroidal Thickness in High Myopic Amblyopia Using Spectral-Domain Optical Coherence Tomography. Front Med (Lausanne). 2022;9:808409.
11. Denison RN, Vu AT, Yacoub E, Feinberg DA, Silver MA. Functional mapping of the magnocellular and parvocellular subdivisions of human LGN. Neuroimage. 2014;102 Pt 2(0 2):358-69.
12. Ryan L, Sun-Yan A, Laughton M, Peron S. Cortical circuitry mediating interareal touch signal amplification. Cell Rep. 2023;42(12):113532.
13. Demirci H, Gezer A, Sezen F, Ovali T, Demiralp T, Isoglu-Alkoc U. Evaluation of the functions of the parvocellular and magnocellular pathways in strabismic amblyopia. J Pediatr Ophthalmol Strabismus. 2002;39(4):215-21.
14. Verghese P, McKee SP, Levi DM. Attention deficits in Amblyopia. Curr Opin Psychol. 2019;29:199-204.
15. Richards MD, Goltz HC, Wong AMF. Audiovisual perception in amblyopia: A review and synthesis. Exp Eye Res. 2019;183:68-75.
16. Richards MD, Goltz HC, Wong AMF. Optimal Audiovisual Integration in the Ventriloquism Effect But Pervasive Deficits in Unisensory Spatial Localization in Amblyopia. Invest Ophthalmol Vis Sci. 2018;59(1):122-131.
17. Putzar L, Goerendt I, Heed T, Richard G, Büchel C, Röder B. The neural basis of lip-reading capabilities is altered by early visual deprivation. Neuropsychologia. 2010;48(7):2158-66.
18. Kothari R, Bokariya P, Singh S, Singh R. A Comprehensive Review on Methodologies Employed for Visual Evoked Potentials. Scientifica (Cairo). 2016;2016:9852194.
19. Bowman R, Foster A. Testing the red reflex. Community Eye Health. 2018;31(101):23.
20. Birch EE, Kelly KR, Wang J. Recent Advances in Screening and Treatment for Amblyopia. Ophthalmol Ther. 2021;10(4):815-30.
21. South J, Gao T, Collins A, Turuwhenua J, Robertson K, Black J. Aniseikonia and anisometropia: implications for suppression and amblyopia. Clin Exp Optom.

2019;102(6):556-65.
22. Verma A. Anomalous adaptive conditions associated with strabismus. Ann Ophthalmol (Skokie). 2007 Spring;39(2):95-106.
23. Herzau V. How useful is anomalous correspondence? Eye (Lond). 1996;10 (Pt 2):266-9.
24. Wong AM, Lueder GT, Burkhalter A, Tychsen L. Anomalous retinal correspondence: neuroanatomic mechanism in strabismic monkeys and clinical findings in strabismic children. J AAPOS. 2000;4(3):168-74.
25. Katsumi O, Tanaka Y, Uemura Y. Anomalous retinal correspondence in esotropia. Jpn J Ophthalmol. 1982;26(2):166-74.
26. Williams C. Pediatric ophthalmology and strabismus. 2nd ed. Br J Ophthalmol. 2004; 88(7):977.
27. Chaturvedi I, Jamil R, Sharma P. Binocular vision therapy for the treatment of Amblyopia-A review. Indian J Ophthalmol. 2023;71(5):1797-803.
28. Wang S, Tian T, Zou L, Wu S, Liu Y, Wen W, et al. Fixation Characteristics of Severe Amblyopia with Eccentric Fixation and Central Fixation Assessed by the MP-1 Microperimeter. Semin Ophthalmol. 2021;36(5-6):360-5.
29. Mishra A, Jackson ML. Translational Vision Rehabilitation: From Eccentric Fixation to Reading Rehabilitation. Semin Ophthalmol. 2016;31(1-2):169-77.
30. Gopal SKS, Kelkar J, Kelkar A, Pandit A. Simplified updates on the pathophysiology and recent developments in the treatment of amblyopia: A review. Indian J Ophthalmol. 2019;67(9):1392-9.
31. Kaur S, Sharda S, Aggarwal H, Dadeya S. Comprehensive review of amblyopia: Types and management. Indian J Ophthalmol. 2023;71(7):2677-86.
32. Chen AM, Cotter SA. The Amblyopia Treatment Studies: Implications for Clinical Practice. Adv Ophthalmol Optom. 2016; 1(1):287-305.

Footnotes and Financial Disclosures

Conflict of interest:

The authors have no conflict of interest with the subject matter of the present manuscript.