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· **Review Article** ·

Research and prospects on the visual mechanisms and treatment modes of amblyopia

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HIGHLIGHTS

· This article summarizes the visual mechanisms and treatment modalities of amblyopia based on the research findings of our group and both domestic and international studies and provides insights into the future development of amblyopia diagnosis and treatment in light of existing challenges.

· Our research group has focused on addressing key scientific issues in amblyopia, including the development of quantitative methods for detecting binocular vision, particularly interocular visual suppression, elucidating the mechanisms of binocular vision impairment in amblyopia, exploring treatment methods and their evaluations, and investigatingvisual plasticity and its neural mechanisms in amblyopia.

· There are still many unknowns regarding the central mechanisms of visual development, impairment, and visual plasticity in amblyopia. The deepening of research on the central mechanisms of amblyopia based on the development of neuroscience is expected to enhance our understanding of visual plasticity. New treatment methods for amblyopia, such as precise anti-suppression treatment and visual training, advanced binocular vision training and reconstruction, repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (t-DCS), are anticipated to bring innovative ideas for the clinical treatment of amblyopia, especially for cases beyond the critical period of visual development, and provide more accurate and personalized treatment strategies and visual reconstruction methods for amblyopia patients.

Abstract: Amblyopia is a neurodevelopmental vision disorder resulting from abnormal visual input during the critical period of visual development, such as strabismus, uncorrected anisometropia, high refractive errors, and form deprivation. It is frequently associated with reduced visual acuity and deficits in binocular vision. Traditional occlusion therapy for amblyopia has typically been restricted to infants

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Full Text

and young children during the critical period of visual development, as it is believed to be ineffective for older children and adults due to the decreased plasticity of the mature brain. Our research group has concentrated on pivotal scientific issues in amblyopia, including quantitative methods for detecting binocular vision, especially interocular visual suppression, the mechanisms underlying binocular vision impairment in amblyopia,treatment methods and their evaluations for amblyopia, and visual plasticity and its neural mechanisms in amblyopia. This paper summarizes the visual mechanisms and treatment modalities of amblyopia based on our research and both domestic and foreign sources, while also looking forward to the future development of this field in light of existing problems.

Keywords: amblyopia; binocular vision; treatment methods; visual plasticity; neural mechanisms

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Amblyopia is a neurodevelopmental vision disorder caused by abnormal visual input during the critical period of visual development, such as strabismus, uncorrected anisometropia, high refractive errors, and form deprivation.[1] Amblyopes experience a range of visual function defects, including poor visual acuity, decreased contrast sensitivity, increased visual crowding effect, and stereoscopic vision impairment, in both monocular and binocular vision.[2-6] Amblyopia is a prevalent neurodevelopmental vision disorder in childhood and a major factor affecting the visual quality of children and adolescents. It not only causes significant visual function damage but also impacts the psychological health and development of children and adolescents.[7] Research indicates that there were 99.2 million amblyopia patients worldwide in 2020, with projections suggesting an increase to 175.2 million by 2030 and 221.9 million by 2040.[8] Depending on the research population, the prevalence of amblyopia in China is about 2% -4%.[9-12] Without timely and appropriate treatment, amblyopia can lead to lifelong deficiencies in visual acuity and stereopsis.

There are three distinct manifestations of amblyopia: deprivation amblyopia, strabismic amblyopia, and refractive or anisometropic amblyopia.Each type is characterized by a unique brain morphology and exhibits differing critical periods for treatment.[13] Simply put,morphological cortical changes have been reported in deprivation amblyopia[14-16] whereas such changes are not typically manifested in strabismic amblyopia or anisometropic amblyopia, as evidenced by anatomical studies.[17-21] However, functional or metabolic cortical changes of different kinds of amblyopia have been revealed by functional MRI studies.[22-24]

Currently, the pathogenesis of amblyopia remains unclear, with imbalanced visual competition and visual suppression between the eyes being considered key factors contributing to visual function impairment in amblyopia.[25-26] However, there is a lack of quantitative detection methods to better elucidate the relationship between the degree of interocular visual suppression and visual function impairment in amblyopia, as well as to characterize the visual impairment in different types of amblyopia. Traditional occlusion therapy for amblyopia has demonstrated good efficacy in children during the critical period of visual development. Nevertheless, challenges such as low treatment efficiency, long treatment cycles, poor patient compliance, reduced efficacy for amblyopia patients beyond the critical period, and the inability to reconstruct advanced binocular vision persist.[1,27] Our research group has focused on addressing key scientific issues in amblyopia, including the development of quantitative methods for detecting binocular vision, particularly interocular visual suppression, elucidating the mechanisms of binocular vision impairment in amblyopia, exploring treatment methods and their evaluations, and investigatingvisual plasticity and its neural mechanisms in amblyopia.This article summarizes the visual mechanisms and treatment modalities of amblyopia based on the research findings of our group and both domestic and international studies and provides insights into the future development of amblyopia diagnosis and treatment in light of existing challenges.

AMBLYOPIA AND INTEROCULAR VISUAL SUPPRESSION

Interocular visual suppression is common in patients with amblyopia. It develops during childhood to prevent image confusion and diplopia and plays a key role in the binocular visual deficits of amblyopes.[28] Clinical methods for evaluating interocular visual suppression include Worth 4 dot point, Bagolini striated glasses, synoptophore, red glass test, etc. However, most of these methods are qualitative analyses that cannot accurately quantify the depth of interocular visual suppression.In recent years, following the proposal of the two-stage theory of binocular interaction[29] and the rapid development of computer technology, numerous quantitative methods for measuring interocular visual suppression based on psychophysics have been introduced, such as the binocular phase combination test and the dichoptic motion coherence test. In the binocular phase combination test, two horizontal sinusoidal gratings of equal contrast but out of phase are presented to the two eyes. To perceive a single image, the contrast of one set of grating bars must be decreased and the amount of contrast decrease is defined as the effective contrast ratio. This ratio indicates the level of interocular visual suppression in amblyopia.[30-31] The dichoptic motion coherence test measures interocular visual suppression by separating a group of moving dots into the signal (coherently moving dots) and noise (randomly moving dots). While the signal's contrast remains constant, the noise's contrast is adjusted. The noise's contrast at which observers barely perceive motion is noted as an index of interocular visual suppression.[32]

To further explore the role of interocular visual suppression in the visual impairment of amblyopia and the characteristics of different types of amblyopia, we applied the dichoptic motion coherence test established by our collaborative team (Professor Robert F. Hess, Professor Chang-Bing Huang) to quantify the strength of interocular visual suppression in both strabismic and anisometropic amblyopes. This test involved using a global motion stimulus where signal elements moving in a coherent direction were seen by one eye, and noise elements moving in random directions were seen by the other eye.[33] We also achieved quantitative measurement of interocular visual suppression based on binocular contrast matching with different spatial distributions. Our findings indicated that the degree of interocular visual suppression is directlycorrelated with the degree of amblyopia, i.e.stronger suppression with a greater difference in interocular acuity and poorer stereo acuity.[33] Furthermore, the distribution of interocular visual suppression is symmetric and appears to be less at greater eccentricities, with the deepest suppression occurring at the foveal area in both the amblyopic and control groups.[34] It is noteworthy that a reduction in interocular visual suppression and strengthening of binocular fusion lead to concomitant improvements in monocular visual acuity of the amblyopic eye and even re-establishing stereopsis.[35-36] Conversely, following the improvement of visual acuity in amblyopia, the degree of interocular visual suppression also significantly decreases.[37] Overall, these research results confirm that interocular visual suppression plays a crucial role in the occurrence, development, and treatment of amblyopia, providing a theoretical basis for precise anti-suppression therapy for different types of amblyopia.

AMBLYOPIA AND ANISEIKONIA

Aniseikonia is a prevalent binocular anomaly where both eyes perceive the same object as exhibiting a different size and/or shape. This inequality in image perception between the two eyes can arise due to significant disparities in ocular optics, retinal receptor distribution, or cortical processing magnification.[38] These differences can lead to a range of adverse visual symptoms, including headache, visual fatigue, photophobia, reading disorders and diplopia.For children during the critical period of visual development, the discrepancy in images between the two eyes caused by aniseikonia may itself be one of the risk factors leading to abnormal interocular suppression, which in turn can result in the development of amblyopia. Currently, the commonly employed methods for measuring aniseikonia in clinical practice include the Space Eikonometer, the New Aniseikonia Test (NAT), and the Aniseikonia Inspector (AI).[39-40] Most aniseikonia tests utilize anaglyphic filters to disassociate targets, which work effectively for individuals with normal binocular vision. However, patients with amblyopia may find it challenging to see targets presented to the amblyopic eye, making direct comparisons of image sizes difficult.

Research has shown that adjusting the contrast and/or luminance of the image presented dichoptically to each eye can overcome interocular visual suppression, allowing both targets to become simultaneously visible. Furthermore, when background luminance changes, the difference in binocularity caused by amblyopia is likely to alter the difference in the image size between the two eyes. Therefore, we established a new method for testing aniseikonia by varying the intraocular contrast differences and luminance backgrounds, and preliminarily evaluated the potential of this test for managing anisometropic amblyopia.We demonstrated an aniseikonia test for anisometropic amblyopia, in which one square with a constant size of 125 pixels was fixed at 100% contrast and was viewed by the amblyopic eye through a stereo shutter goggle while the fellow eye viewed squares with various contrast levels (5%, 10%, 20%, 40%, 80%, or 100%) with an adjustable size. We found that at lower contrast, the amblyopic eye perceived the target to be larger than that viewed by the fellow eye; however, there was no significant difference between 80% and 100% contrast. Besides, there was a significant difference in the contrast-induced aniseikonia between a black background and a white background.[41] We also found that aniseikonia may be one of the important reasons for interocular visual suppression in anisometropic amblyopia, and eliminating suppression can improve the perception of aniseikonia in amblyopia patients.[26] These results establish a more convenient quantitative detection method for aniseikonia in clinical practice, which can assist in the evaluation of clinical visual function in patients with amblyopia due to anisometropia and unilateral aphakia. It can also be applied to the quantitative evaluation of anisometropia during the process of optical therapy (such as frame lens, corneal contact lens correction, artificial lens implantation, etc.) for patients with anisometropic amblyopia and amblyopia with aphakia.

AMBLYOPIA ANDVISUAL CROWDING EFFECT

Visual crowding is a normal visual physiological phenomenon, referring to the impaired ability to recognize an object in clutter, and is considered a significant bottleneck for object recognition and visual awareness in the visual system.[42-45] For normal individuals, peripheral vision is more susceptible to crowding effects, while central vision remains largely unaffected. However, in patients with strabismic amblyopia, crowding effects are also observed in central vision, with objects imaged in the macular fovea demonstrating significant crowding effects.[46-47]

To further investigate the visual crowding effect and its spatial distribution pattern in patients with strabismus and strabismic amblyopia beyond the critical period of visual development, we utilized real-time eye tracking to achieve gaze-contingency and displayed the target and flankers in specific visual field locations. Our finding revealed that the crowding effects in normal individuals are primarily manifested in the peripheral visual field, with relatively balanced crowding effects observed in the nasal and temporal hemifields. However, patients with horizontal concomitant strabismus without amblyopia exhibited stronger crowding effects, demonstrating naso-temporal asymmetry along the radial axis. Specifically, exotropia showed stronger temporal hemifield crowding effects, while esotropia exhibited stronger nasal hemifield crowding effects in both the deviated and fixating eyes, consistent with the direction of eye position deviation and anomalous retinal correspondence. Furthermore, the magnitude of crowding change was related to the duration and degree of strabismic deviation, indicating the presence of hemifield- and axis-specific miswiring of cortical processing in object recognition induced by long-term adaptation to ocular misalignment.[48] In patients with strabismic amblyopia, their amblyopic eyes exhibit enhanced visual crowding effects in both nasal and temporal hemifields, suggesting that strabismic amblyopia may result in more severe and extensive visual suppression and functional impairment in their amblyopia eyes. Additionally, optical realignment (i.e., strabismus surgery) can improve the visual crowding effects caused by long-term eye position deviation in strabismus patients, restore the balance of crowding effects in the nasal and temporal hemifields and promote the recovery of postoperative stereopsis. These results indicate that even for older children and adult strabismus patients who are beyond the critical period of visual development, restoring binocular alignment and coordinated input of binocular information can lead to experience-dependent cortical reconstruction and visual function improvement.[49] Our studies provide a more accurate and reflective evaluation method for assessing visual crowding effects in the central area of the visual field, enabling better evaluate the changes in visual crowding effects before and after amblyopia treatment.

AMBLYOPIA AND BINOCULAR DOMINANCE AND INTER-MODULATION

In amblyopia, there exist aberrant binocular connections between the two eyes. Common methods for detecting binocular rivalry encompass subjective psychophysical tests, including the Worth 4-point test, Bagolini striated glasses, synoptophore, binocular phase combination test, and the dichoptic motion coherence test. We employed the classic binocular rivalry task, which involves presenting an incompatible pair of stimuli to the left and right eyes, inducing competition between the visual inputs from both eyes and enabling participants to provide feedback on perceived visual stimulus features by pressing keys. Binocular dominance was measured based on the dominance duration of each eye and the number of dominance switches between eyes.[50] Additionally, we utilized Steady State Visual Evoked Potential (SSVEPs) technology to objectively measure the binocular interaction and intermodulation in patients with anisometropic amblyopia. Binocular rivalry stimuli were presented to patients using stereo goggles, with a pair of circular checkerboardsconcurrently presented to the fellow eye at 6 Hz and the amblyopic eye at 7.5 Hz, thereby objectively detecting and quantifying the binocular rivalry.[51]

Currently, the primary clinical approach for unilateral amblyopia is monocular occlusion. By patching the fellow eye, the amblyopia eye receives more visual stimulation or training, thereby promoting the recovery of visual acuity. In recent years, studies have found that the balance of binocular dominance in adults changes significantly after short-term complete monocular occlusion. Contrary to the traditional theory of occlusion treatment for amblyopia, the occluded eye gains an advantage after being uncovered.[52-54] Based on these findings, recent investigations have explored the "Inverse Occlusion", involving the patching of the amblyopic eye, to enhance binocular balance, visual acuity, and stereopsis. This approach has been applied in older amblyopic children and adults and has achieved certain results.[52] However, complete inverse occlusion therapy conflicts with the concept of traditional occlusion therapy, and complete occlusion of central vision in amblyopia poses a risk of exacerbating visual function impairment. Addressing these issues, we proposed a short-term peripheral occlusion that preserves central vision (central field of view 10°-15°). Using the classic binocular rivalry task, we found that short-term peripheral occlusion can alter the binocular dominance of central vision in normal adults, allowing the occluded eye to dominate in the short term. This provides a new treatment strategy for amblyopia in older adults.[50] Furthermore, we conducted an electrophysiological investigation utilizing SSVEPs to elucidate the impact of inverse occlusion on neural responses in older children and younger adults with anisometropic amblyopia. We found that short-term monocular deprivation of the amblyopic eye leads to a decrease in interocular visualsuppression from the fellow eye toward the amblyopic eye, while patching the fellow eye demonstrated no significant impact on neural activity. Additionally, we identified a correlation between amblyopic eye visual acuity and the change in interocular visual suppression after short-term inverse occlusion. These results suggest that the severity of amblyopic eye visual acuity is intricately linked to neural plasticity, proposing short-term inverse occlusion as a potential experimental alternative treatment for adolescent and adult patients with severe and refractory anisometropic amblyopia.[55] However, peripheral occlusion and reverse occlusion differ from the classic occlusion mode. Their effects on the monocular and binocular visual functions of amblyopia, long-term safety, and mechanisms for improving visual plasticity still require objective detection methods and further research with larger sample sizes. Unless there is sufficient research evidence and clear research conclusions, it is not advisable to perform reverse occlusion treatment for amblyopia in clinical practice.

BINOCULAR TREATMENT MODE FOR AMBLYOPIA

The classic treatment for amblyopia mainly combines etiological treatment with monocular occlusion, which has proven effective for children with amblyopia during the critical period of visual development. However, there are still challenges, such as long treatment cycles, improvement in visual acuity but potential residual binocular vision impairment (especially binocular fusion and stereopsis impairments), and reduced efficacy for amblyopia patients beyond the critical period of visual development. In recent years, based on the theory of binocular visual suppression in amblyopia, treatment modalities aimed at amblyopia binocular visual suppression, promoting binocular integration, and restoring binocular visual function have gained increasing recognition.[35-36] Our collaborative team has conducted binocular treatment for amblyopia by eliminating interocular visual suppression. Our results demonstrate significant improvement in binocular vision functions across different types of adult amblyopia, with the effects of binocular treatment outperforming those of monocular treatment.[36,56] We also proposed a novel binocular training paradigm involving the presentation of high contrast noise to the fellow eye and gradually decreasing image contrast in the amblyopic eye (High Noise Contrast, HNC), with the aim of actively "nourishing" the amblyopic eye despite strong suppression from the fellow eye. Our HNC approach is related to the monocular contrast detection paradigm, which was found to be effective in enhancing contrast sensitivity and visual acuity in the amblyopic eye, but necessitates strong and sustained interocular visual suppression from the fellow to the amblyopic eye. By comparing the efficacy of the HNC strategy with the traditional tolerable noise contrast (TNC) training strategy in amblyopic patients, we found that while both training strategies can significantly improve visual functions in amblyopia, the HNC approach exhibits a superior effect on the recovery of visual acuity and stereopsis in patients with anisometropic amblyopia beyond the critical period of visual development compared to TNC training. Furthermore, patients who have received the TNC strategy training can still achieve additional improvements in monocular and binocular vision functions through HNC training.[57] Our results indicate that the HNC strategy is closer to the natural visual environment and more efficient than existing TNC strategies, offering a new option for amblyopia binocular training treatment in clinical practice.

Although binocular training treatment for amblyopia, incorporating video games, movies, virtual reality, augmented reality, mixed reality, and similar methods, has demonstrated promising clinical outcomes in non-blind and small sample studies of amblyopia patients both before and beyond the critical period of visual development, it remains to be conclusively established through large-scale randomized clinical trials whether binocular training can replace monocular occlusion therapy for amblyopia patients before the critical period, as well as the treatment effects on adult amblyopia beyond the critical period. Currently, the results of multiple clinical studies are contradictory, and not all results support the notion that binocular training treatment can replace monocular occlusion therapy for amblyopia in clinical practice.[58-62] Kelly et al.[63] conducted a randomized clinical trial involving 28 children with amblyopia aged 4-10 years old and found that binocular vision iPad training has a superior therapeutic effect compared to occlusion therapy with 2 hours per day at a 2-week follow-up. Conversely, Holmes et al.[58] reported that the visual acuity improvement of amblyopic eye with binocular iPad treatment was not as good as with 2 hours of prescribed daily patching in a study of 385 children aged 5-12 years old with amblyopia. Similarly, a randomized clinical trial by the Pediatric Eye Disease Investigator Group (PEDIG) involving 138 children aged 7-12 years old with amblyopia who have received previous treatment for amblyopia other than spectacles did not observe significant improvements in visual acuity and stereopsis after 4-8 weeks of binocular video game training.[62] Manh et al.[60] also documented that the therapeutic effect of binocular dichoptic video game training was not better than that of monocular occlusion in a randomized clinical trial involving older children with amblyopia aged 13-17 years old. It is worth noting that although the methods and foundations of these binocular vision treatments vary,they are all based on dichoptic and contrast-based binocular balancing, with reduced contrast elements seen by the fellow eye, high contrast elements seen by the amblyopic eye, and high contrast background elements seen by both eyes. However, a recent randomized controlled study involving 149 children aged 4-9 years old from Israel and the United States found that 16 weeks of binocular eye-tracking-based amblyopia home treatment (CureSight) was at least as effective as monocular occlusion with part-time patching limited to 2 hours per day.[64] The CureSight treatment uses combined anaglyph glasses and an eye tracker to induce real-time blur around the fellow eye fovea in dichoptic streamed video content.[65] It is also reported that the visual acuity and stereopsis gains following binocular treatment with CureSight were maintained for 1 year without additional treatment.[66] Nonetheless, there are other factors involved in dichoptic training that must be considered before definite results can be declared.[67] In conclusion, these clinical studies suggest that further clarification is needed regarding the evaluation indicators for the visual function benefits of binocular training treatment for amblyopia, the sustainability of visual function improvement, and the underlying mechanisms that enhance visual plasticity.

VISUAL PATHWAYS IMPAIRMENT IN AMBLYOPIA

In the visual system, there are two main categories of classic visual pathways: the magnocellular pathway, which is primarily responsible for low spatial frequency, high temporal frequency, rough stereo vision, and motion visual information; and the parvocellular pathway, which primarily handles visual information related to color, texture, and fine stereoscopic stimuli.[68] Differential effects of abnormal visual experience and treatment on magnocellular and parvocellular pathways may explain some of the visual deficits and treatment failures observed in amblyopia.[69] To investigate the visual pathways impairment in amblyopia, we measured magnocellular and parvocellular-biased contrast response functions in both eyes of anisometropic amblyopes using isolated-check visual evoked potential (icVEP). This method records the steady-state visual evoked potentials in response to isolated-check stimuli, providing an objective measurement of visual functions within magnocellular and parvocellular pathways. Our finding revealed that the signal-to-noise ratios for magnocellular- and parvocellular-biased stimuli presented to the amblyopic eye were reduced. Additionally, the optical treatment led to an increased response to the magnocellular-biased stimuli but not to parvocellular-biased stimuli in the previously uncorrected amblyopic eye. This suggests that visual plasticity may be retained in older children and adults, particularly within the magnocellular pathway, and optical treatment should be considered.[70] Further comparative analysis of amblyopia types indicated that both magnocellular and parvocellular pathway impairments are present in patients with anisometropic amblyopia, whereas only parvocellular pathway impairments are predominant in patients with strabismic amblyopia. These results imply that there may be differences in the visual pathway damage across different types of amblyopia. Distinguishing the characteristics of visual pathway damage in different types of amblyopia is crucial for further elucidating the visual mechanism of amblyopia, especially its central mechanism. It also lays the groundwork for designing targeted visual training methods tailored to the specific characteristics of visual damage observed in different types of amblyopia.

The reception, transmission, and integration of visual information involve not only the retina and visual pathways but also highly complex mechanisms in the visual center, including the functioning of neurons and neural networks. Historically, there has been relatively little research on the mechanisms of visual center damage in amblyopia. However, with the advancement of neuroscience, further research and understanding of these mechanisms in amblyopia are of great significance for deepening our understanding of visual plasticity mechanisms and establishing more effective visual reconstruction methods. The primary visual cortex

(V1) contains a large number of excitatory neurons responsible for processing and integrating binocular visual information, generating preliminary visual images. Additionally, a small portion of gamma-aminobutyric acid (GABA) - inhibitory interneurons regulate excitatory neurons through synaptic connections and other means, forming a local excitation-inhibition balance (E/I) neural network.[71] The E/I balance is considered the primary mechanism by which the visual cortex network adapts to sensory input.[72] Among these interneurons, the basket interneurons that are immune positive for parvalbumin (PV) are the largest group of GABAergic inhibitory interneurons, and their inhibitory effects have been proven to be important targets for triggering critical plasticity in the visual cortex.[73-74] We conducted brief monocular deprivation (MD) in juvenile mice to model amblyopia during the critical period of visual development and found that the excitatory synaptic input of PV-positive interneurons is weakened, thereby reducing the inhibition of excitatory neurons in amblyopia mice. These results imply that PV-positive interneurons may be important targets affecting the E/I balance in the V1 region, and thus participating in the occurrence of amblyopia and limiting visual cortex plasticity. Furthermore, we found that continuous binocular visual training can promote the recovery of visual function in amblyopia mice after the critical period. After binocular visual training, the ocular dominance of excitatory neurons in the V1 area of amblyopia mice returns to normal, the orientation selectivity of visual stimuli increases, and the activity of PV-positive neurons decreases. This suggests that binocular visual training may reduce the activity of PV-positive neurons in the V1 region, leading to reduced inhibition of excitatory neurons and sustained cortical disinhibition, thereby enhancing the ocular dominance plasticity of amblyopia mice beyond the critical period of visual development and improving their visual function. Further research is needed on the role of different visual neurons in visual information processing, integration, and processing, the changes in visual neurons and neural networks during the occurrence and development of amblyopia, how visual training treatment for amblyopia changes the role of neurons and neural networks during the visual function reconstruction, and the mechanism of improving visual plasticity. Only by deepening these understandings can we have a more comprehensive understanding of the pathogenesis of amblyopia, and provide theoretical support and treatment methods for clinical amblyopia treatment, especially for adult amblyopia treatment.

SUMMARY AND PROSPECT

In this article, we summarize and explore the characteristics of visual function impairments and different treatment modes of amblyopia. Currently, traditional occlusion therapy remains the most effective and economical treatment for amblyopia patients during the critical period of visual development. For amblyopia patients beyond the critical period of visual development, the effectiveness of visual perceptual learning in monocular and binocular modes still requires further clinical research verification. Nowadays the diagnosis and evaluation criteria for amblyopia treatment in clinical practice are primarily based on monocular visual acuity. However, the damage to binocular vision functions caused by amblyopia is far more complex and stubborn than the decline in monocular visual acuity. We propose that incorporating binocular vision function, especially stereopsis, into the diagnosis and treatment criteria for amblyopia may provide a more comprehensive evaluation of the disease’s severity and the treatment effect for amblyopia patients. This approach can also help to focus more on the advanced binocular vision damage that may persist after the improvement of monocular visual acuity in clinical practice, enabling further visual training treatment for amblyopia, such as binocular fusion training and stereopsis reconstruction training. Additionally, there are still many unknowns regarding the central mechanisms of visual development, impairment, and visual plasticity in amblyopia. The deepening of research on the central mechanisms of amblyopia based on the development of neuroscience (including basic research and the application of brain imaging technology), is expected to enhance our understanding of visual plasticity. New treatment methods for amblyopia developed using technologies like smart glasses and virtual reality, such as precise anti-suppression treatment and visual training, advanced binocular vision training and reconstruction, repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (t-DCS), are anticipated to bring innovative ideas for the clinical treatment of amblyopia, especially for cases beyond the critical period of visual development, and provide more accurate and personalized treatment strategies and visual reconstruction methods for amblyopia patients.

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None

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None

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