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Binocular treatment of amblyopia

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Address for correspondence:

Abstract

Amblyopia is the most common cause of monocular vision loss in children and population under 40 years, with an estimated prevalence of 1–5%. Amblyopia is caused by a prolonged period of abnormal retinal stimulation due to strabismus (ocular misalignment), anisometropia (refractive imbalance), or both (combined) and leads to functional deficits including reduced contrast sensitivity, poor spatial localization, poor stereovision, and foveal crowding. The present treatments for amblyopia are predominately monocular, aiming to improve the vision in the amblyopic eye. Recent evidence shows that amblyopes possess binocular cortical mechanisms for both threshold and suprathreshold stimuli. Hence, there is an ongoing search for binocular stimulation methods. Detecting the condition early increases the chances of successful treatment and the earlier it is detected, more successful will be the treatment in equalizing vision in both eyes. If it is not treated timely, it can cause permanent loss of vision. This article reviews the recent advances in amblyopia management and how they can be put to clinical practice.

Introduction

Amblyopia is one of the most challenging subspecialties encountered in pediatric ophthalmology. Amblyopia is the most common cause of monocular vision loss in children and population under 40 years, with an estimated prevalence of 1–5%. Amblyopia is caused by a prolonged period of abnormal retinal stimulation due to strabismus (ocular misalignment), anisometropia (refractive imbalance), or both (combined) and leads to functional deficits including reduced contrast sensitivity, poor spatial localization, poor stereovision, and foveal crowding. The pathophysiology of amblyopia is being advanced with the development of newer imaging modalities and increased understanding of the cortical pathways. Newer horizons are being explored in amblyopia management. The recent research has focused on the binocular treatment of amblyopia in contrast to the conventional uniocular patching.

Conventionally, the amblyopia treatment consists of age-appropriate spectacle prescription followed by occlusion or atropine penalization of the better fellow eye. The equivalent efficacy of patching versus atropine penalization was established by the earlier amblyopia treatment studies conducted as randomized controlled trials by the pediatric eye disease investigator group (PEDIG).[1-5] This article reviews the recent advances in amblyopia management and how they can be put to clinical practice.

Need for newer modalities

Occlusion therapy is not free from side effects. Disadvantages can be occlusion amblyopia, functional debilitation, cosmetic blemish, allergic skin rash, recurrence, poor compliance, psychological problems, ocular deviation due to disruption of fusion, and visual decline. Penalization also suffers from potential side effects due to systemic absorption of drug, allergic reactions, and the fact that active inhibition is not eliminated.

A study of moderate and severe amblyopia treatment found approximately 25% of patients under age seven had a recurrence of amblyopia within the 1st year of stopping treatment, and children ages 7–12 had a 7% chance of recurrence (worsening of

two lines of visual acuity).[6,7] This recurrence is more common in patients with severe amblyopia who went from 6 h of patching per day to no patching. In addition, patients with a history of successfully treated amblyopia need continued close monitoring for a recurrence of amblyopia. 54% of children treated at age <3–7 years still demonstrate some amblyopia at age 10 after adequate therapy.[3] In older children, the effect is even less and around 74% of children aged 7–12 years treated with patching, and 80% treated with atropine have some degree of residual amblyopia on long-term follow-up.[4] In children aged more than 17 years, outcomes are even less effective with only one-quarter–one-half of children responding to combined treatment of spectacles and patching depending on whether they had previous treatment or were treatment naïve (respectively).[5] Overall, among 73–90% of amblyopic children, 15–50% fail to achieve normal visual acuity after months or years of treatment.[1-5]

To help prevent recurrence, patients should be weaned off patching therapy. Residual amblyopia is another treatment challenge, considering vision does not improve sufficiently with one treatment for some patients.

Besides the fact that these treatment modalities have dominated the pediatric ophthalmologist world for ages, patient compliance is poor because of the many negative side effects of patching and drops. Furthermore, patching can cause many psychosocial problems when trying to force a child to comply with wearing their eye patch. Kids do not want to wear their eye patch because it impacts their quality of life and atropine drops can cause light sensitivity and disorientation. Even the patient who has done occlusion therapy with good compliance may improve visual acuity in 50–85% of cases, leading to suppression, stereo blindness, and a deficient depth perception in the rest.

Goal of newer treatment strategies

- Perceptual learning
- Visual processing development
- Oculomotor therapy
- Eye–hand coordination training.

Newer Strategies

The exact mechanism of patching therapy is still unclear; however, possible mechanisms include a reduction of interocular suppression or a purely monocular improvement in the processing of signals from the amblyopic eye. Since there is such a poor binocular outcome from patching, it can be concluded that the effects of patching primarily involve monocular mechanisms. Recent studies have shown that amblyopia is a binocular problem caused by active suppression that converts a structurally intact binocular system into a functionally monocular system. One promising approach for the treatment with amblyopia is the combination of patching and perceptual learning (PL) in its many varied forms, for which both monocular and binocular benefits have been documented. It has been shown that loss of binocularity is one of the defining features of amblyopia; therefore, the focus of research in this area has shifted from monocular interventions that involve patching of the fellow eye to approaches that directly target binocular visual function and as the primary therapeutic step. This has led to increased interest in the development of amblyopia treatments that directly address binocular dysfunction by promoting binocular vision and reducing inhibitory interactions within the visual cortex. Evidence suggests that focusing on binocular treatments for amblyopia may prove to be beneficial in both improving vision and possibly improving binocularity. There are many popular software's that are developed nowadays promoting binocular vision therapy with three-dimensional (3D) gaming and at the same time stimulating binocular interaction. Some of these are purely monocular, some are monocular under otherwise binocular conditions, and one is purely binocular, involving dichoptic stimulation and a dichoptic manipulation of contrast to enable simultaneous use of both eyes. These are believed to treat amblyopia not only in children but also in adults.

The first attempt to provide the combination of short-term occlusion (20 min), controlled visual stimulation, and attentive gameplay (noughts and crosses) was the complementary and alternative medicine treatment. Its beneficial effects were later isolated to the short-term nature of the occlusion and the attentive gameplay. A number of hybrid-binocular approaches have been suggested, which are all directed to recovering monocular function under binocular viewing. The aim is to involve the fixing eye in recovery of vision through intensive training/detection of targets presented exclusively to the amblyopic eye.

These treatments are based on these principles:

- Monocular PL,
- Monocular videogame play (VGP) and dichoptic PL/VGP.

PL

"PL" approach involves administering a single visual percept to both eyes simultaneously or under monocular viewing conditions. A number of visual tasks have been explored as a means to apply PL, including Vernier acuity, Gabor detection, positional discrimination, letter identification in noise, position discrimination in noise, and contrast detection.[8] Various studies have reported the beneficial effect of exercises based on PL in adult as well as juvenile amblyopes.[9-14] These positive effects have also been noted to be more on crowding.[15] However, this improvement might be task dependent; based on the type of activity or exercise used. It might be difficult to generalize its benefits in all types of amblyopia. There is no doubt that PL combined with short-term patching is much better than longer-term patching with passive stimulation in terms of improving monocular acuity;[14] however, its usefulness for reestablishing binocular vision and stereopsis is less clear. PL tasks have been done only in laboratory settings and yet have not been extrapolated to home-based settings. These studies have been conducted in small group of patients only in experimental setups. The utility of this principle in a larger number of patients, in a home setting with longer follow-up as randomized studies, is lacking.

Dichoptic training

A dichoptic treatment presents an independent stimulus to each eye in contrast to PL, and the brain is forced to integrate the images into a single perception. In these treatment modalities, under binocular conditions, the task given is such that it requires binocular integration under monocular viewing conditions. The signal strength coming into the patient's good eye is reduced enough so that it cannot suppress the amblyopic eye. The stimuli to the amblyopic eye may be of higher contrast than the fellow good eye. The result is binocular perception in a patient with otherwise deep suppression of the amblyopic eye. Over time, the viewing conditions are changed, and the image seen by the good eye is suppressed less until both eyes see approximately the same image. These tasks have proven to be beneficial both in between and outside the critical period.[16-19] In the first study of its kind by Hess *et al*.,[17] the investigators found that at-home use of the iPod-based game for 10–30 h restored simultaneous binocular perception in 13 of 14 cases along with significant improvements in acuity (0.11 ± 0.08 logMAR) and stereopsis (0.6 ± 0.5 log units). Furthermore, the anaglyph and lenticular platforms were equally effective. In addition, the iPod devices were able to record a complete and accurate picture of treatment compliance. On this basis, they concluded that the home-based dichoptic iPod mobile game approach represents a viable treatment for adults with amblyopia. Other software's based on dichoptic learning also have been found to improve stereoacuity.

The technology was also translated into clinical practice on an iPod-based game which had the disadvantage of requiring a head position[19] and later into red-green dichoptic images making it more generalizable.[20]

Binocular iPad therapies

The principle of dichoptic training was converted to an iPad game and put into a trial by Birch *et al*.[20] The hypothesis was based on the physiological evidence that weak, noisy signals from the amblyopic eye can contribute to binocular vision if suppression by the fellow eye is reduced by signal attenuation, for example, reducing stimulus contrast. There were four binocular iPad games played using red-green anaglyphic glasses. Children had to move and rotate falling blocks to fit them together with base blocks in the falling blocks game. For all four games, amblyopic eye contrast was set to 100% and, initially, fellow eye contrast was set to 15–20%, based on the child being able to play the games successfully during training. They demonstrated a significant improvement in children aged 4–12 years by 4 h of gaming therapy. However, the biggest disadvantage of the study was that patching was not prohibited in the study.

Later on, it was put into a trial in younger children also.[21] PEDIG conducted a randomized control trial comparing 7 days/week and 1 h/day of falling blocks game versus 2 h patching and found them equivalent. However, in the falling blocks game, studies showed a poorer compliance as the children did not feel compelled to play the game for 1 h also.[22-24] In conclusion, the binocular iPad therapy although showed overwhelming results did not prove efficient to be put into clinical practice. A newer study replaced the falling blocks game with the Dig Rush game and demonstrated greater amblyopic eye visual acuity improvement than patching (0.15 LogMAR vs. 0.07 LogMAR).[25]

These games achieve their therapeutic effect by presenting a different image to each eye, thus rewarding the patient when both eyes work together to win the game. For instance, in the stereo block game, some of the blocks seen by the amblyopic eye are in high contrast, while other blocks in lower contrast are seen by the healthy eye. The contrast level in these games can be modified based on each patient's burden of disease. Furthermore, these mobile games are easily available in every smartphone which gives colorful binocular visual stimulus in an entertaining way, which children enjoying without any limitation.

Programmable electronic glasses

The lenses are liquid crystal display; they can also be programmed to turn opaque, occluding vision in the left or right eye for different time intervals, acting like a digital patch that flickers on and off. Amblyz™ occlusion glasses were used for 4 h daily in a study, where the lens over the eye with better vision switched from clear to opaque every 30 s (presented at AAO but not published). These showed promising results, but commercial application of these glasses is still limited.

Interactive Binocular Treatment (I-BiT) for Amblyopia

The I-BiT prototype system was developed as an alternative to patching treatment and utilized a virtual reality technology. The treatment was designed to appeal to children and therefore improve compliance. Computer games and video footage were displayed in such a way that the amblyopic eye of a patient could be preferentially stimulated during binocular viewing conditions.[26] This technology was converted into a computer-based game and 3D shutter glasses in a study.[27] Patients received 30min of I-BiT treatment once a week for 6 weeks, giving a maximal total treatment time of 3 h. Six of nine patients (67%) who completed the treatment showed a clinically significant improvement of 0.125 LogMAR units or more at follow-up of 10 weeks. Thus, this user-friendly treatment provided a small group showing a significant improvement which has to be reproduced in other studies.

Binocular treatment of amblyopia using video games is an ongoing trial to investigate whether 6 weeks of binocular treatment leads to a greater improvement in amblyopic eye visual acuity than 6 weeks of a placebo treatment.[28] The trial will also assess whether binocular treatment improves stereopsis and quality of life, and reduces interocular suppression to a greater extent than placebo treatment. In conclusion, current occlusion therapy, although efficient in recovering the monocular visual acuity of the amblyopic eye, prevents the two eyes from working together. Newer models

believe, patients with amblyopia may have a structurally intact, but functionally suppressed, binocular visual system. Published reports indicate that the learning (or improving) potential is still present in treated amblyopes, who have normal monocular visual acuity and that additional treatment might be necessary. The current research aims at stimulating binocular interaction. The proven advantages of the binocular therapies are (1) contrast balanced binocular treatment improves monocular and binocular visual function in children and adults, (2) the treatment is rapid, working within a matter of weeks, and (3) the effects last in excess of 1 month after the cessation of treatment.

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