Amblyopia: what else beyond patching and critical period?

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Amblyopia has been conventionally defined as “a unilateral or bilateral decrease of visual acuity (VA) caused by pattern deprivation or abnormal binocular interaction, for which no cause could be detected by the physical examination of the eye and which, in some cases, could be reversed by therapeutic measures”1.1 Recent understanding emphasizes that, amblyopia could be redefined as a syndrome, “a visual cacophony of deficits in contrast sensitivity, spatial localization, fixation, ocular motility, accommodation, crowding, attention, motion perception and temporal processing in addition to VA loss”.2

This article aims to review the understanding of amblyopia from the developments in literature in the view of amblyopia mechanisms, treatment and future directions.

Amblyopia is the major cause of defective vision in the young with large population studies showing an amblyopia prevalence of 1.6–3.6% with higher rated in medically underserved population.3 Amblyopia has traditionally been classified as strabismic (SA), anisometropic (AA), refractive or deprivational according to the accompanying conditions thought to be responsible for the acuity loss.4 There is converging evidence in literature that suggests that amblyopia might be more correctly classified in terms of the visual and oculomotor disturbances noted.5

Amblyopia can be defined as a developmental abnormality of the visual cortex.6,7 There may be a loss of connections (under-sampling) or a distortion or rearrangement of connections (neural disarray) within the visual cortex, and this depends on the etiology that caused the amblyopia and the central nervous system compensates to the loss by means of the above-mentioned mechanisms.8 The binocular interactions and the associated deficits are more apparent in the central visual field than the periphery,9,10 and the inhibitory mechanisms are active under binocular viewing.11

The art of amblyopia treatment lies in balancing the conflicting demands of monocular and binocular vision. During the past 20 years, different critical periods have been demonstrated for different visual functions during the development of the visual system.1,2 Critical period is that sensitive period in the life span of an organism where the skills acquired are indispensable. It is believed that, visual functions processed at higher anatomical levels within the system have a later critical period than functions processed at lower levels.13

Binocular function and stereopsis, if disrupted within this sensitive period, are difficult to retrieve at later age. This general principle suggests that the treatment for amblyopia should follow a logical sequence, with treatment for each visual function starting before its critical period is over.8 Three periods in the development of the visual system in human infants have been postulated by Daw.8 These include a pre-stereoptic period (0–4 months), onset of stereopsis (4–6 months) and post-stereoptic period (6 months–2yeaars). These functions are all plastic for a period after they first develop.

Based on the understanding of critical period, it could be predicted that anomalous binocular visual experience during early infancy severely disrupts stereopsis. Fawcett et al.14 used a random dot stereo test to determine the critical period for stereopsis in infantile and accommodative strabismus in children <5 years of age and found that the critical period for susceptibility of stereopsis extends through late infancy and early childhood and continues to at least 4.6 years of age. In more than 200 years, there is better understanding of the neurophysiology and neuropathology of amblyopia than the past, though the treatment has not changed significantly.15 The mainstay of treatment still consists of forcing the use of the amblyopic eye, most often by occlusion of the sound eye and is probably the oldest treatment modality. Either Saint-Yves in 172216 or de Buffon (1743) is credited with the first documentation of occlusion treatment for amblyopia. There has been adequate research on standardizing the occlusion regimens that ranges from a few minutes of patching a day to all waking hours, often continuing for many months.17 More successful treatment strategies are being opted currently through well controlled experiments and neurophysiologic research, and recent randomized controlled trials have tried to answer the basic questions, “which of the two eyes should be occluded, and with what, and for how long?”18,19

There is a variety of evidence from the literature that the eye contralateral to the amblyopic eye, referred to as the good eye has subtle but measurable deficits in a wide variety of visual functions.3 In this context, we (Varadharajan & Hussaindeen, 2012)20 tried to understand the development of VA in the better eye of unilateral amblyopes. A total of 112 children with amblyopia were included (SA, 14; AA, 51; combined...
Dichoptic training. This leads to restoration of substantial degree of plasticity. The primary suggests that matured amblyopic brain retains a sensitive period of development but newer studies more slowly than in healthy control patients. We concluded through this study that VA in the fellow eye of children with unilateral amblyopia is reduced at baseline and matures more slowly than in healthy control patients.

Moving on to visual plasticity, it was believed that adult amblyopia is irreversible beyond the sensitive period of development but newer studies suggests that matured amblyopic brain retains a substantial degree of plasticity. The primary sensory cortex also remains plastic in adulthood and perceptual learning (PL) could be of benefit in restoring the visual functions of the adult amblyopic system. PL refers to experience-induced changes in the way perceivers extract information and plays a larger role in complex cognitive tasks. A new approach of binocularly based treatment modality that provides measurement and treatment of suppressive imbalance as a first step is Dichoptic training. This leads to restoration of stereoscopic function along with reduction in the monocular acuity deficit. Ultimately, it strengthens the binocular vision by eventually combining binocular information under natural viewing conditions (stimuli of the same contrast in each eye). However, PL as well as Dichoptic training needs a controlled environmental set up as well as large number of trials.

An alternate or a simpler strategy to this approach would be Action Videogames (AVG) that can be used as a home-based therapy in any environmental setup. It provides visually enriched environment with extraordinary speed, constant monitoring of the periphery, tracking of fast moving objects, perceptual, cognitive and/or motor skills, ignoring distracters and aiming small moving targets. For training amblyopic eyes, we need a task that trains many visual functions at a time. Video games might be able to fit into such a criterion. AVG exercise has shown to improve VA, potential acuity, spatial attention and stereoaucity in adults with amblyopia.

We tried to understand the efficacy of AVGs in improving the visual functions in adult amblyopia. This study carried out at Sankara Nethralaya had two main goals: to assess whether AVGs can improve visual performance in adult and juvenile amblyopes; to assess the sustainability (retention) of visual functions after cessation of the exercise. A total of 36 subjects (age: 13–31 years) were recruited and allocated into two intervention groups: AVG group (n = 33) and Conventional Patching group (n = 8). Crowded VA, uncrowded VA, stereo acuity, contrast sensitivity and degree of suppression were measured in each visit. Visual functions were reassessed after 20th and 40th hour of AVG exercise. Retention of these visual functions was assessed after 1, 5 and 7 months of cessation of the exercise. After 80 h of occlusion, no significant improvement of visual functions was noted in conventional patching group (P > 0.05). Twenty-one subjects who completed 40 h of AVG exercise showed substantial improvement of VA (median improvement: 0.16 log MAR; uncrowded: 41.02% and crowded: 27.6%), contrast sensitivity (maximum improvement at four cycles/degree: 113.2%), stereo acuity and depth of suppression. The AA and CMA groups showed speeder recovery of VA as compared to the SA group. Improvement of VA not only sustained fully, but also improved further after 5–7 months of cessation.

These results suggest that AVGs can be administered for active vision training in adult and juvenile amblyopes after the critical period. Ours is the first study to report regarding sustainability of the improvements obtained. Improvement of VA not only sustained well in mild and moderate amblyopes, but also revealed further improvement. Overall improvements in CS almost fully retained for 1 and 5 months post cessation at maximum spatial frequencies and was above 76% after 7 months of cessation. These results show a lot of promise toward newer treatment strategies such as video games and dichoptic training for amblyopia beyond patching and beyond the critical period. Dichoptic training seems to be the future of amblyopia treatment considering the advantages that it renders to both the monocular and binocular visual system in amblyopia. Hence, it is time for a well-planned randomized controlled trial assessing the efficacy of these modern treatment approaches in improving the visual functions in adult and juvenile amblyopes compared to conventional treatment strategies.

References
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