Visual Acuity Improvement in Adult Anisometropic Amblyopes After Active Vision Therapy

Leila Sharbatoghi\textsuperscript{1}  
Hassan Hashemi\textsuperscript{2}  
Alireza Mohamadi\textsuperscript{3}  
Ebrahim Jafarzadehpur\textsuperscript{3}  
Abbasali Yekta\textsuperscript{4}  
Ali Mirzajani\textsuperscript{3}  
Mehdi Khabazkhoob\textsuperscript{5}  

\textsuperscript{1}Noor Research Center for Ophthalmic Epidemiology, Noor Eye Hospital, Tehran, Iran; \textsuperscript{2}Noor Ophthalmology Research Center, Noor Eye Hospital, Tehran, Iran; \textsuperscript{3}Rehabilitation Research Center, Department of Optometry, School of Rehabilitation Sciences, Iran University of Medical Sciences, Tehran, Iran; \textsuperscript{4}Refractive Errors Research Center, Mashhad University of Medical Sciences, Mashhad, Iran; \textsuperscript{5}Department of Medical Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran, Iran

\textbf{Purpose:} The aim of this study is to evaluate the effect of active vision therapy in adults with anisometropic amblyopia.

\textbf{Methods:} In this study, 20 adults with anisometropic amblyopia aged from 17–35 years old were treated for five sessions (one session per week) with vision therapy techniques which include accommodative rock, vergence rock, and saccadic training. Moreover, computerized vision therapy was performed by Optosys\textsuperscript{6} software. Also, patients had been given a daily program for home training, including accommodative and vergence rock, and Optosys\textsuperscript{6} software. Best corrected visual acuity (BCVA) was measured before and after treatment.

\textbf{Results:} Comparison of data using \textit{t}-test showed that BCVA significantly improved after the vision therapy period. Initial BCVA (Log MAR) was 0.37±0.04 (mean±standard deviation) which improved to 0.14±0.03 after treatment. The correlation between initial BCVA and the amount of improvement showed that the worse the pre-treatment visual acuity was, the greater improvement that occurred.

\textbf{Conclusion:} The improvement of visual acuity in adult anisometropic amblyopes showed that there are some degrees of plasticity in the visual system of amblyopic patients even in adulthood. Thus, therapists should give the chance of treatment to adult amblyopes.

\textbf{Keywords:} anisometropic amblyopia, plasticity, visual acuity, adult

\textbf{Introduction}

Amblyopia is the most common form of unilateral or sometimes bilateral decrease in best corrected visual acuity (BCVA) that is not related to any structural or pathological disorder in the visual system. However, it is due to abnormal visual experiences such as strabismus, anisometropia, and visual deprivation in early childhood.\textsuperscript{1} Clinically, amblyopia is referred to a decrease in BCVA for at least two lines of visual acuity charts (monocularly or binocularly). This disorder is the most common cause of worldwide unilateral blindness which has affected 3–5% of the world population.\textsuperscript{1}

In the past it was thought that adult amblyopia could not be treated, possibly due to the reduced cortical plasticity. According to this view, treatment was not suggested to adult patients. However, more recent studies revealed that cortical plasticity continues in adulthood, although it is not as plastic as in childhood.\textsuperscript{2} There is some plasticity at the stages of synapses and cortical cells, that results in the ability to repair the defected areas in the visual cortex. So, adults are able to improve sensory activities by perceptual learning and practice. This kind of learning may have an effect on the cortex.\textsuperscript{2}

Levi\textsuperscript{2} reported a significant improvement in visual acuity of adult amblyopic patients. Khan’s\textsuperscript{3} experiment showed significant improvement after vision training for amblyopic patients with a mean age of 17.
Generally, treatments of amblyopia include optical correction of refractive error, occlusion therapy, and active amblyopia therapy.4 The success rate of occlusion therapy varies between 60–80%.5,6 However, passive treatment methods such as occlusion and medical or optical penalization are still be a major part of treatment, although they are not always successful and sometimes have non-persistent results specially for strabismic amblyopia.7,8 Most of the patients do not have normal binocularity after treatment in spite of good visual acuity.9 Lack of development of binocular vision results in a lack of visual skills in adulthood. Nowadays, this disorder is treated by a vision specialist, because amblyopia is a neural disorder that is caused by abnormal brain stimulation in a sensitive period of vision development.9 So, it is necessary to know the neural mechanism of amblyopia to find out more effective treatment strategies. More recent amblyopia treatment methods, using some stimuli as an active therapy, may activate some special areas of the visual cortex.10 There are a lot of active amblyopia treatment methods.11 However, their effectiveness has not been fully tested.12,13 Since there is a considerable population of adult amblyopes who did not receive proper treatment in childhood and considering the importance of adult amblyopia therapy for education and occupation, we decided to evaluate the effect of active therapy on adult anisometropic amblyopia patients.

Method
This study was performed on 20 patients with anisometropic amblyopia aged from 17–35, who had been referred to the orthoptic clinic at Noor eye hospital. They had never previously had eye surgery or vision therapy. Also they were pathologically and neurologically healthy and did not use any medicine. Visual acuity (Log MAR) of the patients was measured with the best refractive correction by Nidek system Chart SC-1600 (Nidek Co., Aichi, Japan). The improvement of best corrected visual acuity (BCVA) was compared before and after the therapy period. Each patient had five successive sessions for training in one session per week schedule. At the end of this period, their best corrected visual acuity was measured. The treatment program in each session included 5 minutes of each of these trainings: accommodative rock with ±2.00 flipper lenses, vergence rock with 4Δ base in/12Δ base out flipper prisms, training for improving fixation with Haidinger’s brushes and intermittent photic stimulation (3 Hz frequency flashing of a small and colorful picture) by Synoptophore (Haag-Streit Clement Clark 2001 model, Essex, UK), and computerized training of eye–hand coordination and Dynamic Meridional Visual Stimulation (DMVS) by Optosys® software (Farakavosh inc. Tehran, Iran). Moreover, a daily home vision training program was given to patients including: 2 hours per day occlusion of the non-amblyopic eye, 5 minutes of accommodative rock with far and near Accommodative Rock Cards and computerized eye-hand coordination and DMVS by Optosys® software as explained for office training. The patient should do this training three times a day. Neurologic experiments showed that neurons in the visual cortex can be activated by grating stimuli. Color-opponent high contrast grating that change their orientation, spatial frequency, and colors continuously is the basis of DMVS training. In office accommodative and vergence rock we used a target that is one line better than the patient’s BCVA at 40 cm. After the 5 week period of therapy, the improvement in BCVA of the patients was evaluated by paired t-test analysis. SPSS software (IBM SPSS, Armonk, NY, USA) version 22.0 was used for statistical analysis and a P-value<0.05 was considered as significant.

Ethical Approval
All procedures performed in studies involving human participants were in accordance with the ethical standards of the Iran University of Medical Sciences research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. All patients signed a written informed consent form.

Results
From 27 patients who participated in this study, seven did not accomplish the treatment, and thus were excluded from the study. The study continued with the remaining 20 patients (eight females and 12 males). The age range of participants was 17–35 years old with mean±standard deviation (SD) (22.65±6.31). Best corrected visual acuity of all patients but one increased after treatment (Figure 1). T-test showed that post-treatment BCVA (0.14±0.03) was significantly better than pre-treatment BCVA (0.37±0.04) (P<0.001).

To examine the relationship between pre-treatment visual acuity and the amount of improvement, we used Spearman correlation test. The result showed that the worse pre-treatment visual acuity was the greater improvement that occurred (P<0.001) (Figure 2).
Many visual skills such as accommodation, vergence, and contrast sensitivity are affected in amblyopic patients. Studies showed that amplitude and facility of accommodation is diminished in amblyopic patients.14 The diminished accommodative response in amblyopia can be improved after vision therapy.15 The sensation of vergence disparity is also defected in strabismic amblyopes.16

A decrease in amplitude of saccades in amblyopic patients has been reported in the study of Niechwiej-Szwe et al,17 where the visual processing in a sensory system operates slowly for amblyopic eyes. Accurate eye–hand coordination needs normal binocular vision. Thus, decreased stereopsis perception in monocular amblyopia is one of the most important reasons of diminished eye–hand coordination.18 Optosys® software is beneficial for saccadic eye movements, eye–hand coordination, and improvement of the function of magno- and parvo-cellular systems. Dynamic Meridional Visual Stimulation (DMVS) is one of the Optosys® training options specially designed to improve contrast sensitivity by affecting magno and parvo systems. The chance for achieving 20/20 visual acuity (VA) is considerably more for the amblyopic eyes with 20/40 or better pre-treatment VA.19-21 The prognosis is weaker for strabismic amblyopia than anisomeric amblyopia.

Duration of treatment directly relates to age. Thus, older patients may need longer treatment periods. However, strabismic amblyopes with eccentric fixation may need prolonged treatment duration even if the patient is a preschool aged child.22 Kupfer reported that seven adults with strabismic amblyopia aged 18–22 improved significantly while their normal eye had been occluded during fixation training. Based on this result we can conclude that there is no age limitation for visual acuity improvement.23 There are two mechanisms of amblyopia therapy in adults, 1) activation of the suppressed neural synapses that are normal but suppressed, and 2) learning to pay more attention and training for accomplishing a difficult visual task.8

According to previous studies, there are two major pathways in the human visual system to process visual information that may be affected in amblyopia.24-26 The parvocellular (P) pathway includes smaller cells which are specialized in fine and color information. The magnocellular (M) pathway includes larger cells which are more sensitive to motion and changes in stimuli. Moreover, M cells are responsive to high contrast, while P cells are sensitive to low contrast.27 The

Discussion
This study shows that vision therapy has successful results on adults with anisometric amblyopia. Based on the results, visual acuity improved significantly in adults after vision training (Figure 1). This result has been approved in similar studies.2 The correlation test was used to evaluate the relationship between the initial visual acuity and the amount of improvement. As shown in Figure 2, the initial visual acuity was negatively correlated to the amount of improvement. Since our participants did not suffer from disorders such as eccentric fixation or binocular disruptions, we could also see significant improvement in severe amblyopia cases, which approves the presence of cortical plasticity in adults.

Figure 1 Comparison of pre- and post-treatment visual acuity.

Figure 2 The correlation between the initial visual acuity and the amount of improvement.
P pathway will be affected in mild amblyopia, and the M pathway will be involved too if the amblyopia is deep.28 Contrast sensitivity is normal in low spatial frequency stimuli in amblyopic eyes. However, decreased contrast sensitivity in higher spatial frequency, reflects a defect in the P system. Recent studies showed that most of the amblyopic eyes have decreased contrast sensitivity just in high spatial frequencies, and some of them with more severe amblyopias show decreased contrast sensitivity in all spatial frequencies which is due to the malfunction of both P and M systems.28–33 Thus, activation of the P and M cells may improve the chance of success in amblyopia therapy. Using high spatial frequency and colored stimuli in DMVS training activates the P system, while lower spatial frequencies and changing the orientation of the grating activates the M system.

Obviously the traditional treatment of amblyopia is patching the non-amblyopic eye in order to improve the visual acuity in the amblyopic eye. However this method could not selectively stimulate either of the visual pathways. Furthermore, with occluding one eye during the treatment, binocular vision would be disrupted. Thus, active amblyopia therapy will be a more complete treatment method. In conclusion, the results of this study showed improvement of visual acuity in adult anisometropic amblyopia patients, which reflects the visual neural system plasticity in adults. We can conclude that active amblyopia therapy would be advantageous for adult amblyopes. We suggest that further research should be done to find out the age limits of active therapy for adults in older age groups and other types of amblyopia.

Disclosure
The authors report no potential conflicts of interest for this work. The authors alone are responsible for the content and writing of the paper.

References
1. Committee AAoOPPP. Preferred practice pattern guidelines. Comprehensive Adult Medical Eye Evaluation–2010 Available from: http://wwwone aaorg/preferred-practice-pattern/comprehensive-adult-medical-eye-evaluation–octobe. Accessed February 2015, 26.
2. Levi DM. Perceptual learning in adults with amblyopia: a reevaluation of critical periods in human vision. Dev Psychobiol. 2005;46:222–232. doi:10.1002/dev.20500
3. Khan T. Is there a critical period for amblyopia therapy? Results of a study on older anisometropic amblyopes. J Clin Diagn Res. 2015;9: NC01–04.
4. Rouse MW, Cooper JS, Cotter S, Press L, Tannen B Optometric clinical practice guideline: care of the patient with amblyopia. Available from: http://wwwaoaorg/documents/optometrists/CPG-4pdf2004.
5. Group PED. A randomized trial of atropine vs patching for treatment of moderate amblyopia in children. Arch Ophthalmol. 2002;120(3):268. doi:10.1001/archophthalmol.120.3.268
6. Loudon SE, Polling JR, Simonsz HJ. Electronically measured compliance with occlusion therapy for amblyopia is related to visual acuity increment. Graefes Arch Clin Exp Ophthalmol. 2003;241:176–180. doi:10.1007/s00417-002-0570-z
7. Buch H, Vinding T, La Cour M, Nielsen NV. The prevalence and causes of bilateral and unilateral blindness in an elderly urban Danish population. The Copenhagen City Eye Study. Acta Ophthalmol Scand. 2001;79:441–449. doi:10.1034/j.1600-0420.2001.790502.x
8. Stewart CE, Fielder AR, Stephens DA, Moseley MJ. Treatment of unilateral amblyopia: factors influencing visual outcome. Invest Ophthalmol Vis Sci. 2005;46(9):3152–3160. doi:10.1167/iosvs.05-0357
9. Wong AM. New concepts concerning the neural mechanisms of amblyopia and their clinical implications. Can J Ophthalmol. 2012;47:399–409. doi:10.1016/j.jjcojo.2012.05.002
10. Suttle CM. Active treatments for amblyopia: a review of the methods and evidence base. Clin Exp Optom. 2010;93:287–299. doi:10.1111/j.1444-0938.2010.00486.x
11. Schor C, Gibson J, Hsu M, Mah M. The use of rotating gratings for the treatment of amblyopia: a clinical trial. Am J Ophthalmol Physiol Opt. 1981;58:930–938. doi:10.1097/00000632-198111000-00004
12. Schor C, Wick B. Rotating grating treatment of amblyopia with and without eccentric fixation. J Am Optom Assoc. 1983;54:545–549.
13. Mitchell DE, Howell ER, Keith CG. The effect of minimal occlusion therapy on binocular visual functions in amblyopia. Invest Ophthalmol Vis Sci. 1983;24:778–781.
14. Ciuffreda KJ, Rumpf D. Contrast and accommodation in amblyopia. Vision Res. 1985;25:1445–1457. doi:10.1016/0042-6989(85)90223-8
15. Ciuffreda K, Hokoda S, Hung G, Semmlow J. Accommodative stimulus/response function in human amblyopia. Documenta Ophthalmologica. 1984;56:303–326. doi:10.1007/BF00155676
16. Kenyon RV, Ciuffreda KJ, Stark L. Dynamic vergence eye movements in strabismus and amblyopia: symmetric vergence. Invest Ophthalmol Vis Sci. 1980;19:60–74.
17. Niechwiej-Szwedo E, Goltz HC, Chandrakumar M, Hirji ZA, Wong AM. Effects of anisometropic amblyopia on visuosensor behavior: I: saccadic eye movements. Invest Ophthalmol Vis Sci. 2010;51:6348–6354. doi:10.1167/iovs.10-5882
18. Suttle CM, Melmoth DR, Finlay AL, Sloper JJ, Grant S. Eye-hand coordination skills in children with and without amblyopia. Invest Ophthalmol Vis Sci. 2011;52:1851–1864.
19. Jam Polsky A, Flom BC, Weymouth FW, Moses LE. Unequal corrected visual acuity as related to anisometropia. AMA Arch Ophthalmol. 1955;58:893–905. doi:10.1001/archophthalmol.1955.90003020899013
20. Kivlin JD, Flynn JT. Therapy of anisometropic amblyopia. J Pediatr Ophthalmol Strabismus. 1981;18:47–56.
21. Tanlalmai T, Goss DA. Prevalence of monococular amblyopia among anisometropes. Am J Ophthalmol Physiol Opt. 1979;56:704–715.
22. Ho CS, Giaschi JD, Boden C, Dougherty R, Cline R, Lyons C. Deficient motion perception in the fellow eye of amblyopic children. Vision Res. 2005;45:1615–1627.
23. Kuper C. Treatment of amblyopia. Ex Anopsia in Adults Am J Ophthalmol. 1957;43:918–922. doi:10.1016/0002-9394(57)91795-6
24. Polat U, Bonneh Y, Ma-Naim T, Belkin M, Sagi D. Spatial interactions in amblyopia: effects of stimulus parameters and amblyopia type. Vision Res. 2005;45:1471–1479. doi:10.1016/j.visres.2004.12.014
25. Simmers AJ, Edgeway T, Hess RF. The influences of visibility and anomalous integration processes on the perception of global spatial form versus motion in human amblyopia. Vision Res. 2005;45:449–460. doi:10.1016/j.visres.2004.08.026
26. Zele AJ, Pokorny J, Lee DY, Ireland D. Anisometric amblyopia: spatial contrast sensitivity deficits in inferred magnocellular and parvocellular vision. *Invest Ophthalmol Vis Sci.* 2007;48:36 22–3631. doi:10.1167/iovs.06-1207

27. Davis AR, Sloper JJ, Neveu MM, Hogg CR, Morgan MJ, Holder GE. Differential changes of magnocellular and parvocellular visual function in early- and late-onset strabismic amblyopia. *Invest Ophthalmol Vis Sci.* 2006;47:4836–4841. doi:10.1167/iovs.06-0382

28. Bradley A, Freeman R. Contrast sensitivity in anisometric amblyopia. *Invest Ophthalmol Vis Sci.* 1981;21:467–476.

29. Bradley A, Freeman RD, Applegate R. Is amblyopia spatial frequency or retinal locus specific? *Vision Res.* 1985;25:47–54.

30. Chatzistefanou KI, Theodossiadis GP, Damanakis AG, Ladas ID, Moschos MN, Chimonidou E. Contrast sensitivity in amblyopia: the fellow eye of untreated and successfully treated amblyopes. *J AAPOS.* 2005;9(5):468–474. doi:10.1016/j.jaapos.2005.05.002

31. Hess RF, Howell ER. The threshold contrast sensitivity function in strabismic amblyopia: evidence for a two type classification. *Vision Res.* 1977;17(9):1049–1055. doi:10.1016/0042-6989(77)90009-8

32. Levi DM, Harwerth RS. Spatio-temporal interactions in anisometric and strabismic amblyopia. *Invest Ophthalmol Vis Sci.* 1977;16:90–95.

33. Völkers A, Hagemans K, Van Der Wildt G, Schmitz P. Spatial contrast sensitivity and the diagnosis of amblyopia. *Br J Ophthalmol.* 1987;71:58–65. doi:10.1136/bjo.71.1.58