

Video Article

Stereoacuity Improvement using Random-Dot Video Games

Santiago Martín-González¹, Juan Portela-Camino², Javier Ruiz-Alcocer³, Igor Illarramendi-Mendicute⁴, Rafaela Garrido-Mercado⁵¹Department of Construction and Manufacturing Engineering, University of Oviedo²Department of Optometry, Clinic Begira³Department of Health Sciences, Complutense University of Madrid⁴Department of Optometry, Begitek Clinic⁵School of Optometry, Complutense University of MadridCorrespondence to: Santiago Martín-González at martinsantiago@uniovi.esURL: <https://www.jove.com/video/60236>DOI: [doi:10.3791/60236](https://doi.org/10.3791/60236)

Keywords: Behavior, Issue 155, amblyopia, stereopsis, video games, random-dot, perceptual learning, compliance

Date Published: 1/14/2020

Citation: Martín-González, S., Portela-Camino, J., Ruiz-Alcocer, J., Illarramendi-Mendicute, I., Garrido-Mercado, R. Stereoacuity Improvement using Random-Dot Video Games. *J. Vis. Exp.* (155), e60236, doi:10.3791/60236 (2020).

Abstract

Conventional amblyopia therapy involves occlusion or penalization of the dominant eye, though these methods enhance stereoscopic visual acuity in fewer than 30% of cases. To improve these results, we propose a treatment in the form of a video game, using random-dot stimuli and perceptual learning techniques to stimulate stereoacuity. The protocol is defined for stereo-deficient patients between 7-14 years of age who have already received treatment for amblyopia and have a monocular best corrected distance visual acuity of at least 0.1 logMAR. Patients are required to complete a perceptual learning program at home using the video game. While compliance is stored automatically in the cloud, periodic optometry center visits are used to track patient evolution and adjust the game's stereoscopic demand until the smallest detectable disparity is achieved. The protocol has proved to be successful, and effectiveness is gauged in terms of a two-level gain on a random stereoacuity test (global stereoacuity or cyclopean stereoacuity reference test). Moreover, the random-dot stimuli learning transfers to medial lateral stereoscopic acuity according to a Wirt Circles test, in which success criteria is a final stereoacuity of over 140", and the attained enhancement corresponds to no less than two levels of stereoscopic acuity. Six months later, a random-dot stereoacuity test recorded no reduction in the stereoacuity that was achieved.

Video Link

The video component of this article can be found at <https://www.jove.com/video/60236/>

Introduction

Amblyopia is a developmental disorder of spatial vision frequently associated with the existence of strabismus, anisometropia, or form deprivation at a young age¹. The incidence of amblyopia among the general population ranges from 1.3%-3.6%². Conventional amblyopia therapy starts with the correction of any refractive error, followed by occlusion of the good eye with a patch or atropine penalization³. Although treatment outcomes of conventional treatment are initially good, with 73%-90% of patients experiencing improved visual acuity, this improvement does not equate to normal visual acuity in about 50% of patients. Moreover, children frequently experience deterioration even after successful treatment². A previous study showed that, with respect to binocular vision, as few as 28% of anisometropic patients with amblyopia recorded two or more levels of improvement as a result of treatment⁴. There has been little research aimed at evaluating strategies for the improvement of stereopsis in cases of amblyopia, despite the fact that stereopsis is essential to visual perception in humans⁵. Conventional amblyopia therapy, which produces good results for visual acuity but poor outcomes in terms of binocular vision, can benefit from the development of an interventional model aimed at improving stereoacuity in patients with a history of amblyopia².

Over the last 10 years, some researchers have proposed an alternative approach to understanding the course of amblyopia^{6,7}. This understanding has motivated the proposal of a interventional model focused on anti-suppression dichoptic training for the recovery of binocular vision^{8,9}. Amblyopia therapy involving targeted gamified activities for patient use at home has been reported successful in a number of cases^{10,11}.

Notwithstanding, this dichoptic training is ineffective for improving stereoscopic acuity¹². Two contemporary clinical trials using the anti-suppression dichoptic training model reported no stereoacuity improvement^{11,13}. The most recent research indicates, however, that dichoptic stimulation is capable of reducing suppression depth and extent and improving binocular vision (restoring simultaneous binocular perception). In some cases, this coincides with improved stereoacuity^{14,15}.

Some studies have proposed a different intervention approach that is focused on the direct stimulation of stereopsis through perceptual learning activities^{16,17}. These studies are confined to a succession of cases treated under laboratory conditions. In Astle et al.'s study, stereopsis was stimulated in two adult anisometropic amblyopes¹⁶ over the course of nine laboratory sessions. Treatment included binocular stimulation using a mirror stereoscope with stereogram pairs based on random-dot images. Ding and Levi stimulated stereopsis in a course of treatment conducted entirely under laboratory conditions, using a mirror stereoscope and stereograms based on Gabor patches¹⁸. Their subjects were five adults,

four of which having no stereopsis and one being stereo-deficient. Subjects were required to perform between 3,000-20,000 perceptual learning training trials.

Furthermore, Xi et al. studied anisometropic amblyopes over the course of 10 -13 perceptual learning training sessions, during which 3-D anaglyph textures were used to stimulate stereopsis¹⁹. Finally, in Vedamurthy et al.'s study, 11 stereo-deficient adults were engaged in visuo-motor task training (a "squash-the-bug" game) in a virtual reality environment¹⁷. These subjects performed 12,600 trials in 35 sessions over the course of 8-11 weeks.

Direct stimulation of stereopsis has been performed in laboratory studies, but this therapy model is time-consuming and difficult to apply in a daily clinical practice, especially with children. Thus, a feasible therapy model has been devised for which a successful proof of concept has been previously presented²⁰. This protocol incorporates the results of a prospective, randomized, double-blind, parallel-group study based on perceptual learning treatment using random-dot stimuli in a video game format to improve stereoacuity. An in-depth explanation of the protocol followed in this study is presented.

Protocol

The study design was approved by the Basque Country Ethics Committee and followed the tenets of the Declaration of Helsinki. Written informed consent was obtained either from participants enrolled in the study or their legal guardians. **Figure 1** represents the protocol steps.

1. Participant Recruitment

1. Recruit patients with the following characteristics: between 7-14 years of age with refractive amblyopia and/or successfully treated strabismic amblyopia (strabismus children are only eligible to participate if misalignment of the visual axes has been successfully corrected with glasses, visual therapy, and/or strabismus surgery); with monocular best corrected distance visual acuity of ≥ 0.1 logMAR²¹; and stereoacuity measured in the 800"-200" range (coarse-moderate stereo-deficiency)²² according to a random-dot stereogram test²³.
 1. To determine "refractive amblyopia", consider the interocular refractive difference error by means of autorefraction under cycloplegia. NOTE: Anisometropic amblyopia is defined when a patient presents an interocular refractive difference error of ≥ 1 spherical dioptre (D), (spherical equivalent). Isometropic amblyopia is defined when the cycloplegic refractive error in each eye of ≥ 4.00 D hypermetropia or myopia and/or ≥ 2.00 D astigmatism and the interocular refractive difference error is < 1 D.
 2. To determine successfully treated strabismic amblyopia, check for the absence of strabismus using a monocular cover-uncover test and stimulating accommodation with a letter acuity score of 20/30 to ensure that the subject looks at the letter with the fovea when performing the fixing movement²⁴.
2. Exclude patients with the following characteristics: strabismus; hyperphoria (upward deviation) of 2 prism diopters or more; nystagmus; hypermetropic anisometropia, in which the patient presents a spherical equivalent difference between the eyes of 3 diopters (or more) if corrected with glasses (to prevent aniseikonia); any ocular pathology; attention-deficit/hyperactivity disorder; and any cognitive disorder. Exclude patients without access to a computer or without internet connection at home.

2. Visual Evaluations

1. Perform the Baseline Optometric Evaluation prior to beginning this section for collection of baseline data and ensure all appropriate inclusion/exclusion criteria.
 1. Measure best corrected distance visual acuity (BCVA) with Early Treatment Diabetic Retinopathy Study (ETDRS visual acuity chart).
 2. Check for the absence of strabismus as explained in step 1.1.2.
 3. Measure stereoacuity at a constant distance of 40 cm, under light illumination of 120 cd/m². NOTE: Illumination control guarantees contrast consistency between dots and background in the test pattern. Patient head-to-test distance is a critical variable because it is included in the equation that sets stereoacuity result.
 1. Measure global stereoacuity with a random-dot stereogram (to avoid monocular cues) conducted according to the test manufacturer's instructions.
 2. Measure local stereoacuity using a contour test despite the presence of monocular cues with a Wirt Circles test conducted according to the test manufacturer's instructions.
 4. Measure the refractive error by cycloplegic refraction (1% cyclopentolate) following Pediatric Eye Disease Investigator Group (PEDIG) guidelines^{25,26}.
 5. Rule out any ocular pathology with an in-depth study of the anterior (slit lamp) and posterior (indirect ophthalmoscope) poles.
2. Conducting the optometric center first visit with patients.
 1. Create a patient profile in the game service application.
 1. Set the patient's user identifier and password.
 2. Set the patient's interpupillary distance.
 2. Install the computerized stereoscopic game on the patient's computer.
 3. Configure the game by clicking on the configuration panel.
 1. Set the physical dimensions of the patient's computer screen.
 2. Ensure that the user is wearing the anaglyph glasses correctly (with the red filter over the left eye).
 4. Measure the patient's stereopsis basal acuity using the computerized stereoscopic game.
 1. Ask the patient to play the game under supervision, as explained in section 3.4.

2. Consult the result stored in the cloud using the game service application.
5. Using patient stereopsis basal acuity, set the patient's basal level in the game service application.
 1. The computerized stereoscopic game defines three stimulation categories, each associated with a stereoscopic acuity interval value: poor (840"-300"), coarse (480" -210") and moderate-fine stereopsis (300" -30"). Patients begin with the finest level at which they can identify the stereopsis stimulus. For example, in a patient with a stereo threshold of 720", assign the poor stereopsis level on the patient's profile.
6. Explain to participants how to perform the exercises at home, as explained in section 3.
3. Perform check-up visits on completion of every 15 therapy sessions with the computerized stereoscopic game during the training period.
 1. Open the game service application, open the patient profile and check both compliance and stereopsis results data.
 1. Remind parents and participants about the importance of respecting the working distance from the screen.
 2. Remind parents and participants about the importance of compliance.
 2. Evaluate the logMAR BCVA at distance with an ETRDS test to check for any deterioration from the starting values.
 3. Measure the patient's stereopsis acuity using the computerized stereoscopic game (step 2.2.4)
 4. Set the patient's basal level in the game service application (step 2.2.5).
4. Perform the final optometric evaluation on completion of 60 therapy sessions with the computerized stereoscopic game (end of treatment) to collect outcome data.

NOTE: This evaluation reproduces the baseline optometric evaluation, stressing the measurement of global and local stereopsis.
5. Perform the follow-up optometric evaluation 6 months after completion to ensure stability of the results.

NOTE: This evaluation reproduces the baseline optometric evaluation, stressing the measurement of global and local stereopsis.

3. Treatment Exercises Performed at Home

1. Explain to participants that they must follow a course of training using the computerized stereoscopic game at home for sixty 8 min sessions.
2. Explain that each session must be performed on a different day and that five sessions per week must be completed. Explain to patients that the research team will have access to their compliance and results data in the cloud.
3. Instruct patients to visit the optometry center for a check-up visit after every 15 sessions, which should be completed within 3 weeks to consider compliance as 100%, and in all cases, within a maximum of 6 weeks.
4. Explaining how to use the computerized stereoscopic game
 1. Ask the participant to sit at a distance of 80 cm from the computer screen. Make it clear that patients should not try to cheat the program by moving closer to the screen.
 2. Ensure that the room is dimly lit, avoiding any reflections on the computer screen.
 3. Explain that the program takes the form of a videogame, in which a random-dot image conceals a hidden silhouette. The silhouette can only be seen in three dimensions while wearing anaglyph glasses.
 4. Give the patient a pair of anaglyph glasses and explain how to wear them, focusing on which filter goes to which eye (with the red filter over the left eye).
 5. Provide the patient with an identifier and password to log in to the game (step 2.2.1).
 6. Instruct the patient to use the mouse to select which silhouette appears, selecting one figure from the four options shown at the bottom of the screen (**Figure 2**).
 7. Explain what happens after the selection of a silhouette.
 1. If the answer is correct, the software emits a high-pitched sound, and the correct image appears in the form of a full-color picture as a reward.
 2. If the answer is incorrect, the software emits a deep sound. The player still has two more attempts to find the right answer.
 3. If there are three consecutive wrong answers, the software will show the correct answer.
 8. Explain to the patient that after each trial, the software generates a new screen with a random-dot image concealing a new hidden silhouette.
 9. Explain to the patient that the hidden silhouette becomes more difficult to find as the session progresses and that this is normal.
 10. Explain to the patient that, once the session is complete, the software stores the outcomes in a cloud server, allowing the optometrist to track compliance and stereoacuity evolution remotely.

NOTE: Stress the importance of a stable Wi-Fi connection and of closing the computerized stereoscopic game properly.

Representative Results

As a representative example of the results that can be achieved following this protocol, we summarize the results of a recent study carried out by Portela et al.²⁰. **Figure 3** and **Figure 4** show the outcomes that were obtained.

Sixteen stereo-deficient subjects aged between 7-14 years of age were included in this study, four of whom had a history of refractive amblyopia (2 anisometric and 2 isometric). Twelve of the subjects had a history of successfully treated strabismic amblyopia, and four of these had a history of both strabismic and anisometric amblyopia. Eleven of the 12 subjects with a history of strabismic amblyopia presented esotropia, and one presented exotropia. All participants had previously received amblyopia therapy and achieved good levels of visual acuity but did not attain a fine level of stereoacuity (less than or equal to 200"). All but one of the subjects were able to complete the 60 assigned training sessions that were 8 min each (8 h in total). Compliance was considered to be 100% when patients completed the training in less than 12 weeks and 0% when the training took more than 24 weeks. On average, subjects took 79 days to complete the 60 sessions (IQR = 66-102 days); therefore, they surpassed the minimum recommended compliance of five sessions per week. Compliance outcomes were excellent (88.36%).

Visual acuity among the subjects remained stable during and post-therapy. Stereoacuity, however, improved in a significant number of subjects (see **Figure 3**). The means, medians, and minimum and maximum values are presented in **Table 1**. When these were analyzed using the Mann-Whitney U test, stereoacuity improved significantly after treatment (Random-Dot Stereoacuity test, $p = 0.019$; Wirt Circles test, $p = 0.014$). For a better understanding, **Figure 4** shows a graphic presentation of the improvement in stereoacuity between the start and end of therapy.

Stereoacuity improved by at least one level in 11 subjects when stereoacuity was measured with the random stereoacuity test. Where stereoacuity was evaluated with the Wirt Circles test, improvement of at least one level was also observed in 11 subjects. Clinically speaking, an improvement in stereoacuity measured with a random stereoacuity test is significant when the improvement reaches at least two levels (Adam's criteria)²⁷, and this was achieved in seven subjects. Where the Wirt Circles test was used, an improvement of at least two levels and a stereoacuity equal or better than 140" is considered significant (Levi's criteria)¹², and this was achieved in 10 subjects. After 6 months, the outcomes were stable according to the random-dot stereoacuity test. This is the reference test to measure stereoacuity, with its main feature being its excellent test-retest reliability²³.



Figure 1: Protocol steps. [Please click here to view a larger version of this figure.](#)

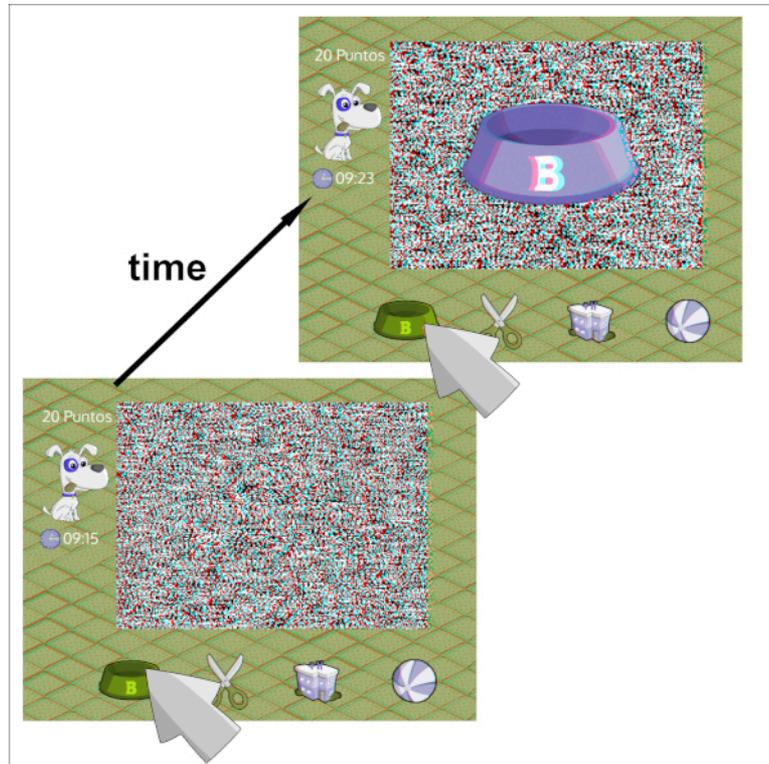


Figure 2: Logical process of the game. The subject must indicate which figure appears, selecting one from those shown at the bottom of the screen (left image). If the answer is correct, the software emits a high-pitched sound, and the same image appears in picture form (right image). If the subject provides three consecutive correct answers, the software generates a new screen with a random-dot image representing a finer stereopsis. If the subject provides a wrong answer, the software emits a deep sound and the random-dot image remains the same (left image). Finally, if the subject provides three consecutive wrong answers, the software will show the correct answer (right image). This figure is adapted from Portela et al.²⁰ with permission from Optometry and Vision Science. [Please click here to view a larger version of this figure.](#)

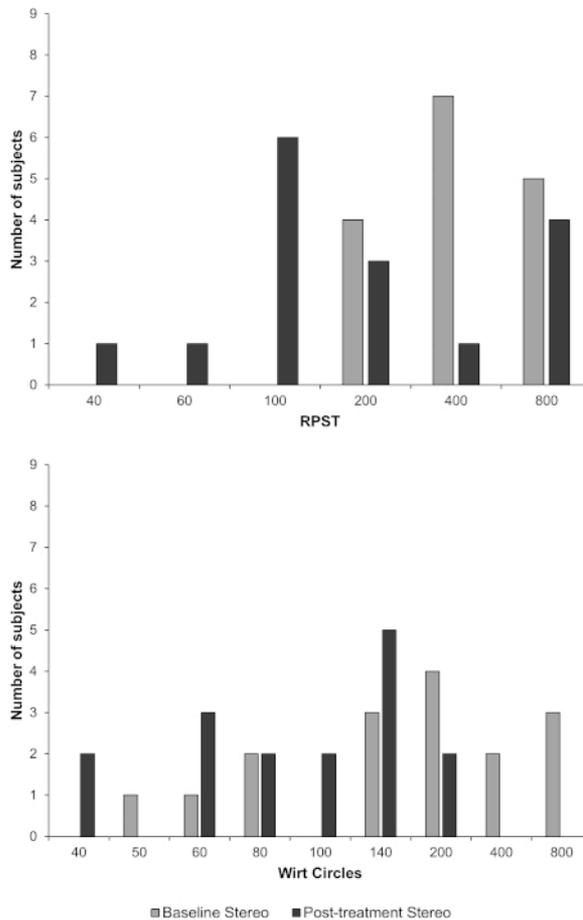


Figure 3: Measurements of basal and post-treatment levels of stereoacuity. Random-dot stereoacuity (RDS) and Wirt Circles tests were used to measure stereoacuity. Measurements are in log seconds of arc. This figure is adapted from Portela et al.²⁰ with permission from Optometry and Vision Science. [Please click here to view a larger version of this figure.](#)

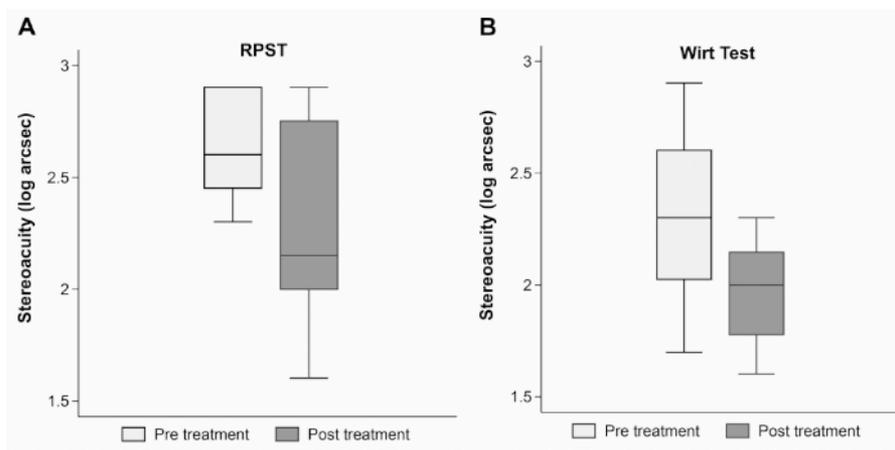


Figure 4: Medians of stereoacuity data before and immediately post treatment for each stereoacuity test. (A) Random-dot stereoacuity (RDS) test and **(B)** Wirt Circles test. Boxes indicate 25% and 75% quartiles. Measurements are in log seconds of arc. This figure is adapted from Portela et al.²⁰ with permission from Optometry and Vision Science. [Please click here to view a larger version of this figure.](#)

	Baseline Stereo		Post-Treatment Stereo	
	Wirt	RST	Wirt	RST
Mean	293.13±271.17	475.00±240.84	107.50±51.60	305.63±306.50
Median	200 [95 to 400] 95%	400 [250 to 800] 95%	100 [60 to 140] 95%	150 [100 to 700] 95%
Min	50	200	40	40
Max	800	800	200	800

Table 1: Means, standard deviation, medians, interquartile ranges, and maximum and minimum stereoacuity values. The left columns show baseline stereoacuity data, and the right columns show post-treatment stereoacuity outcomes. Stereoacuity was measured using random-dot stereoacuity (RDS) and Wirt Circles tests. Measurements are in seconds of arc. This figure is adapted from Portela et al.²⁰ with permission from Optometry and Vision Science.

Discussion

Presented here is a protocol for the direct stimulation of stereoacuity, in which random-dot stereo images are used to enhance stereoscopic acuity in stereo-deficient subjects. Four preceding studies have evaluated the results of direct stimulation^{16,17,18,19}. This latest protocol contributes additional features to the abovementioned interventional models.

The model of intervention proposed is intended for patients with a history of strabismic or anisometropic amblyopia, who have already received treatment (i.e., optical correction, occlusion, strabismus surgery, vision therapy) and achieved a best corrected visual acuity of at least 0.1 logMAR, but whose stereoacuity remains low (between 200"-800"). The goal of the protocol is to improve stereoacuity in cases like these.

Direct stimulation of stereopsis has already been shown to be effective in enhancing stereoacuity in stereo-deficient subjects^{16,17,18,19}. However, for a stimulation system to be feasible, therapy must be performed in the patient's home to reach the 3,000-20,000 trials needed for learning to occur.

In the previously published study that validated this procedure and is summarized above, 11 subjects improved their stereoacuity²⁰. However, five of the subjects experienced no increase in stereoacuity (**Figure 3**). This may be attributable to the presence of small-angle strabismus undetectable in a cover test. Read inferred that, since images from the left and right eyes should be located within Panum's area of fusion, normal stereoacuity should require alignment within 0.6 prism diopters²⁸. Panum's fusional area is ±5-20 min of arc (0.1-0.6 prism diopter in the fovea), and it may be that alignment within this window is needed to support high-grade stereoscopic acuity²⁹. A study conducted by Holmes et al. showed that a cover test failed to detect deviations below ±3 prism diopters; therefore, the presence of undetectable strabismus could compromise a patient's ability to acquire fine stereoacuity²⁴.

Gamification has been used to enhance patient motivation and compliance. Moreover, the program stores data in the cloud after each session, making it possible for the practitioner to track a patient's activity remotely on a daily basis. Thanks to this feature, compliance results are excellent (88.36%) and comparable to those recorded in two earlier studies, in which amblyopic subjects received dichoptic stimulation treatment using an iPad at home^{10,11}. They are also much better than the reported results of a PEDIG study under similar conditions, in which only 22.5% of the sample managed to complete over 75% of the treatment prescribed¹³. The compliance demonstrated here also exceeds that reported by studies that evaluated the effectiveness of occlusion treatment in amblyopia (70% compliance when 6 h of occlusion are prescribed, and 50% when 12 h are prescribed)³⁰. A web application has the added advantage that parents are not required to keep a record of their child's compliance¹³. The optometrist's only duty is to access the server and check the data collected for each patient at the end of each session using the computerized stereoscopic game program.

During the training period, patients visit the optometry center (check-up visits), allowing the optometrist to stress the importance of user-to-screen distance. Optometrists also set the stimulation category (poor, coarse, moderate-fine) during these check-up visits. Perceptual learning theories predict that improvements are less likely if the patient does not work at his or her threshold (e.g., if the patient moves closer to the screen or works in an easier stimulation category). These findings were corroborated in the study carried out to validate this protocol²⁰. User-to-screen distance is out of the software's control and is therefore the responsibility of the patient or patient's parents.

The decision to use a random-dot approach for the design of the computerized stereoscopic game may be critical. Stimulation through random-dot stereoscopic images is never inconsequential: even patients working below their threshold experience improvements. In a process of perceptual learning, repeated exposure to a random-dot stimulus alone will enhance binocular vision. The patient's task, and one that is particularly difficult for patients with a history of strabismus³¹, is to fuse the correlated random dots perceived by each eye¹² without suppression. This enhances their ability to distinguish the correlated dots (signal) from those unable to be fused (noise). Training of this type may have improved the disparity detector response, given that the perceptual learning would have improved the fusional response and improved the patient's ability to detach the signal from noise³².

One of the risks of the perceptual learning approach is selectiveness. This method has demonstrated that random-dot stereogram training is not selective, because learning is transferred to medial lateral stereoacuity measured with a Wirt Circles test. Another finding that demonstrates the effectiveness of this treatment method is the stability of the results achieved. Different studies have examined whether improvements achieved in subjects with amblyopia as a result of perceptual learning training are stable^{16,17,19,33}. This model has demonstrated the stability of the improvements measured with a random-dot stereoacuity test at a 6 month follow-up visit.

Several limitations have been detected. The software design requires the stimulation category to be set manually, when this process should ideally be automatic according to the patient's evolution. The pass level condition implemented could be improved by considering the possibility of moving the patient back to a coarse stereoacuity setting if the patient fails to pass a level on several consecutive occasions. In any case,

a staircase procedure is discarded, because one of the goals of gamification is to improve patient motivation through game mechanics. The patient should experience the sensation of progress and success, regardless of whether their clinical condition is improving or deteriorating. This is achieved by concealing easier trials within the game flow (though not with a standard staircase procedure, whose goal is to quickly and accurately determine the threshold limit, at which performance is 50%). Another improvement is to monitor the patient's distance from the screen automatically. However, we are not aware of a solution that does not involve the use of special hardware, though it may be worth testing custom-built webcam head-tracking software.

Other limitations are due to the study design and include the following: (1) the majority of subjects had a history of strabismus (the sample of subjects with a history of anisometropic amblyopia was too small); (2) the age range was restricted to 7-14 years; and (3) the stereoacuity range was between 800"-200". In future studies, it would be interesting to verify the therapeutic effect on anisometropic amblyopia and coarser stereoacuity and in older subjects.

Disclosures

The computer-based test was developed at the University of Oviedo by S.M.-G., who is a co-author of this manuscript. Subsequent to completion of this study, VISIONARY TOOL, S.L. (found at <www.visionarytool.com>), a private entity, approached S.M.-G. and J.A.P.-C. with an opportunity to take part in the development of a computerised visual training tool, which includes several games and tests, one of which is the random-dot hidden silhouette game used in this article.

Acknowledgments

The authors wish to acknowledge the VISUALIA visual therapy clinic, which partially supported the development of the computer-based test, under agreement with the University of Oviedo (FUO-EM-104-12).

References

- Ciuffreda, K. J., Levi, D. M., Selenow, A. *Amblyopia: Basic and Clinical Aspects*. Butterworth-Heinemann. 1-64 (1991).
- Birch, E. E. Amblyopia and binocular vision. *Progress in Retinal and Eye Research*. **33**, 67-84 (2013).
- Repka, M. X., Holmes, J. M. Lessons from the amblyopia treatment studies. *Ophthalmology*. **119**, 657-658 (2012).
- Wallace, D. K. et al. Stereoacuity in children with anisometropic amblyopia. *Journal of American Association for Pediatric Ophthalmology*. **15**, 455-461 (2011).
- O'Connor, A. R., Tidbury, L. P. Stereopsis: are we assessing it in enough depth? *Clinical and Experimental Optometry*. **101**, 485-494 (2018).
- Mansouri, B., Thompson, B., Hess, R. F. Measurement of suprathreshold binocular interactions in amblyopia. *Vision Research*. **48**, 2775-2784 (2008).
- Farivar, R., Thompson, B., Mansouri, B., Hess, R. F. Interocular suppression in strabismic amblyopia results in an attenuated and delayed hemodynamic response function in early visual cortex. *Journal of Vision*. **11**, 1-12 (2011).
- Hess, R. F., Thompson, B., Baker, D. H. Binocular Vision in Amblyopia: Structure, Suppression and Plasticity. *Ophthalmic and Physiological Optics*. **34**, 146-62 (2014).
- Vedamurthy, I. et al. A dichoptic custom-made action video game as a treatment for adult amblyopia. *Vision Research*. **114**, 173-187 (2015).
- Li, S. L. et al. A binocular iPad treatment for amblyopic children. *Eye*. **28**, 1246-1253 (2014).
- Kelly, K. R. et al. Binocular iPad Game vs Patching for Treatment of Amblyopia in Children: A Randomized Clinical Trial. *JAMA Ophthalmology*. **134**, 1402-8 (2016).
- Levi, D. M., Knillm D. C., Bavelier, D. Stereopsis and amblyopia: A mini-review. *Vision Research*. **114**, 17-30 (2015).
- Holmes, J. M. et al. Effect of a Binocular iPad Game vs Part-time Patching in Children Aged 5 to 12 Years With Amblyopia: A Randomized Clinical Trial. *JAMA Ophthalmology*. **134**, E733-41 (2016).
- Kelly, K. R., Birch, E. E. Binocular outcomes following binocular treatment for childhood amblyopia. *Investigative Ophthalmology & Visual Science*. **59**, 1221-1228 (2018).
- Webber, A. L., Wood, J. M., Thompson, B. Fine Motor Skills of Children With Amblyopia Improve Following Binocular Treatment. *Investigative Ophthalmology & Visual Science*. **57**, 4713-4720 (2016).
- Astle, A. T., McGraw, P. V., Webb, B. S. Recovery of stereo acuity in adults with amblyopia. *BMJ Case Reports*. 1-4 (2011).
- Vedamurthy, I. et al. Recovering stereo vision by squashing virtual bugs in a virtual reality environment. *Philosophical Transactions of the Royal Society B*. **37**, 20150264 (2016).
- Ding, J., Levi, D. M. Recovery of stereopsis through perceptual learning in human adults with abnormal binocular vision. *Proceedings of the National Academy of Sciences of the United States of America*. **108**, E733-41 (2011).
- Xi, J. et al. Perceptual Learning Improves Stereoacuity in Amblyopia. *Investigative Ophthalmology & Visual Science*. **55**, 2384-91 (2014).
- Portela-Camino, J. A. et al. A Random Dot Computer Video Game Improves Stereopsis. *Optometry and Vision Science*. **95**, 523-535 (2018).
- Birch, E. E. et al. Risk Factors for Esotropic Amblyopia. *Investigative Ophthalmology & Visual Science*. **48**, e1108 (2007).
- Leske, D. A., Birch, E. E., Holmes, J. M. Real depth vs randot stereotests. *American Journal of Ophthalmology*. **142**, 699-701 (2006).
- Fawcett, S. L., Birch, E. E. Interobserver test-retest reliability of the Randot preschool stereoacuity test. *Journal of American Association for Pediatric Ophthalmology*. **4**, 354-8 (2000).
- Holmes, J. M., Leske, D. A., Hohberger, G. G. Defining real change in prism-cover test measurements. *American Journal of Ophthalmology*. **145**, 381-385 (2008).
- Cotter, S. A. et al. Treatment of anisometropic amblyopia in children with refractive correction. *Ophthalmology*. **113**, 895-903 (2006).
- Cotter, S. A. et al. Treatment of strabismic amblyopia with refractive correction. *American Journal of Ophthalmology*. **143**, 1060-1063 (2007).
- Adams, W. E. et al. Defining real change in measures of stereoacuity. *Ophthalmology*. **116**, 281-285 (2009).
- Read, J. C. A. Stereo Vision and Strabismus. *Eye*. **29** 214-224 (2015).

29. Birch, E. E., Wang, J. Stereoacuity outcomes after treatment of infantile and accommodative esotropia. *Optometry and Vision Science*. **86**, 647-652 (2009).
30. Stewart, C. E. et al. Objectively monitored patching regimens for treatment of amblyopia: randomised trial. *British Medical Journal*. **335**, 707 (2007).
31. Westheimer, G. Clinical evaluation of stereopsis. *Vision Research*. **90**, 38-42 (2013).
32. Gantz, L. et al. Mechanisms of Perceptual Learning of Depth Discrimination in Random Dot Stereograms. *Vision Research*. **47**, 2170-8 (2007).
33. Zhou, Y. et al. Perceptual learning improves contrast sensitivity and visual acuity in adults with anisometropic amblyopia. *Vision Research*. **46**, 739-750 (2006).