An iPod treatment for amblyopia: An updated binocular approach

¹⁴ [2] **R.F.** Hess, D.Sc., ^a **B.** Thompson, Ph.D., ^b J.M. Black, O.D., ^b G. Maehara, Ph.D., ^a ¹⁶ [2] **P.** Zhang, ^c W.R. Bobier, Ph.D., ^c L. To, Ph.D., ^d and J. Cooperstock, Ph.D.^d

^aDepartment of Ophthalmology, McGill University, Montreal, Canada; ^bDepartment of Optometry and Vision Science, University of Auckland, New Zealand; ^cSchool of Optometry, University of Waterloo, Waterloo, Canada; and ^dCenter for Intelligent Machines, McGill University, Canada.

Abstract We describe the successful translation of computerized and space-consuming laboratory **KEYWORDS** equipment for the treatment of suppression to a small handheld iPod device. A portable and easily Suppression; 25[Q2]obtainable Apple iPod display, using current video technology offers an ideal solution for the clinical Amblyopia; treatment of suppression. The following is a description of the iPod device and illustrates how a video Strabismus; game has been adapted to provide the appropriate stimulation to implement our recent antisuppression Binocular vision treatment protocol. One to 2 hours per day of video game playing under controlled conditions for 1 to 3 weeks can improve acuity and restore binocular function, including stereopsis in adults, well beyond the age at which traditional patching is used. This handheld platform provides a convenient and effective platform for implementing the newly proposed binocular treatment of amblyopia in the clinic, home, or elsewhere. Optometry 2012; ■:1-8

binocular function that should be corrected first with the as-

sumption that the amblyopia will reduce as a consequence.

This idea gains support, as recently we have shown that

suppression is a fundamental aspect of the visual deficits

that characterize strabismic and anisometropic amblyo-

pia.²⁻⁴ This work has also shown that understanding and mea-

suring suppression is key to the management of these

conditions and to the restoration of binocular function. We

have argued that suppression not only renders what is struc-

turally a binocular visual system, functionally monocular in

the case of strabismic and anisometropic amblyopia, but also

makes a significant contribution to the monocular amblyopic

loss.^{1,2} Furthermore, we have shown that suppression can be

quantified using a dichoptic motion task and can be system-

atically reduced with training under conditions that ensure

the combination of information between the 2 eyes of an

amblyopic observer.⁴ This simple antisuppression training

It has long been assumed that the primary anomaly in strabismic and anisometropic amblyopia is a monocular visual loss and that the loss of binocular function follows as a consequence. This is why patching was instigated, but it is commonly found that the restoration of binocular function does not follow as a consequence of correcting amblyopia.¹ It is quite possible that this current way of thinking is not correct. It may well be that the primary deficit is the loss of binocular function and that the monocular loss of vision fol-lows as a consequence of this. If this is correct, it is the

49 Disclosure: This work was supported by an I2I NSERC grant to JC and
 50 RFH and a University of Auckland FRDF grant to BT and JB. The author,
 51 through McGill University has applied for patents for both the iPod device and treatment method.

52 * Corresponding author: Robert F. Hess, D.Sc., Department of Ophthal-

- 53 mology, McGill University, Montreal, Canada, H3A1A1.
- 54 E-mail: Robert.hess@mcgill.ca

56 1529-1839/\$ - see front matter © 2012 American Optometric Association. All rights reserved.

57 doi:10.1016/j.optm.2011.08.013

172

173

174

175

176

177

178

179

180

181

182

183

184

185

186

187

188

189

190

191

192

193

194

195

196

197

198

199

200

201

202

203

204

205

206

207

208

209

210

211

212

213

214

215

216

217

218

procedure can restore stereopsis in a large number of cases
and will result in significant reductions in the degree of
monocular amblyopia, even in adults well beyond the age
at which patching treatment is adopted.^{2,3}

Initially, we used a laboratory approach with computer 119 120 screens and a mirror haploscope and time-consuming but rigorous psychophysical measuring procedures.⁴ This led to 121 122 the development of a compact head-mounted display where 123 organic light-emitting diode screens mounted before each 124 eye provided controlled, convenient dichoptic stimulation and a more abbreviated testing procedure.⁵ We have now 125 taken this a stage further and implemented our measurement 126 127 [Q3] and treatment regime on a handheld Apple iPod device. Such a device can be used without any other viewing appa-128 129 ratus to measure the degree of suppression in a strabismic or 130 anisometropic amblyopia and to provide the type of stimula-131 tion environment needed to restore binocular function as 132 well as a degree of monocular function in amblyopic individ-133 uals. Because the device is portable and pocket size, it can be conveniently used outside the clinic. To enhance its appeal 134 and acceptability with the younger age group, where the 135 136 treatment will be most effective, we have implemented the 137 training procedure as a Tetris video game. 138

139 Rationale

140 We have previously shown, using random dot stimuli and a 141 dichoptic motion task, that information is combined between 142 the 2 eyes of an amblyope when the contrast of the signal 143 seen by the fixing eye is sufficiently reduced compared with 144 that seen by the amblyopic eye.⁴ This, we argue, is because 145 the suppressive drive from the fixing eye is contrast depen-146 dent. Furthermore, we have shown that prolonged viewing 147 under these artificial conditions, in which the fixing eye 148 contrast is reduced, leads to a strengthening of binocular 149 vision in strabismic amblyopes, which is reflected in eventu-150 ally being able to combine interocular signals of equal 151 contrast.^{2,3} In our video game platform, we constructed a 152 stimulus composed of elements seen by one or the other 153 eve (i.e., a dichoptic Tetris stimulus), and ensured that the 154 game could only be played successfully if the information 155 from the 2 eyes was combined (i.e., ensuring that there 156 was binocular combination or fusion). We achieved this by 157 reducing the contrast of the elements seen by the fixing 158 eye, which, in turn, reduced the suppression of the amblyo-159 pic eye. Over time, if the game is played successfully, the 160 contrast of the elements seen by the fixing eye can be 161 increased with the aim of eventually eliminating the contrast 162 offset between the eyes so that binocular combination can 163 take place under unaided natural viewing conditions. 164

$\frac{165}{166} [\mbox{Q4}]$ Methods

167

168 System implementation

169

170 *Display calibration and settings.* We used a second-171 generation iPod with its screen brightness set to about half the maximum level, at approximately 150 cd/m², with [Q5] autobrightness turned off. The iPod screen has a resolution of 480 \times 320. The game information is presented in gray-scale mode, with all color channels having the same pixel value. At the moment, there is little benefit for adding a finer luminance resolution control, such as bit stealing, because the viewing conditions for this device can vary significantly between participants.

To measure the nonlinearity of the grayscale luminance to produce on-screen contrast, we approximated the iPod luminance output using the following gamma model

$$L_{out} = L_{\min} + (L_{\max} - L_{\min}) \left(\frac{y}{255}\right)^{\gamma}$$

where L_{max} and L_{min} are the maximum and minimum luminance of the iPod screen, $y \square [0,255]$ is the pixel value assigned to all channels, and γ represents the display nonlinearity. To estimate γ , we measured the luminance output over the range [0,255], and then fitted a gamma curve through the sampled data.

The Tetris game is presented on a midgray background. At any given moment in the game, there are 2 contrast levels on display. The contrast for each block is calculated as follows:

$$C = \frac{L_{foreground} - L_{background}}{L_{background}}$$

where $L_{\text{foreground}}$ is the luminance of the game block, and the background luminance $L_{\text{background}} = L_{\text{max}}/2$. When the game contrast changes, the foreground luminance and its corresponding gray level are recalculated and updated.

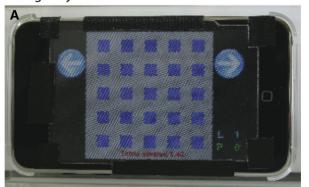
Alignment. Because of the optical method by which dichoptic viewing is achieved, it is important that the iPod is aligned correctly with the subject's eyes. We achieve this by displaying a grid of colored squares, which, when correctly aligned, are perceived to be green by one eye and blue by the other. This is illustrated in Figure 1, where we show the left and right eye views of a correctly aligned iPod. If the iPod is not correctly aligned, the squares seen by either eye are not of uniform color (i.e., green or blue). There is no significance to the actual colors, they are just markers of alignment.

Software

The Tetris game is developed with Objective-C and 219 OpenGL using the iPhone software development kit. Each [Q6] 220 game screen sends 2 independent pictures simultaneously 221 to the eyes. The 2 stimuli are combined into 1 interlaced 222 223 image at the level of the display and are then redistributed to each eye separately via the lenticular screen overlay. 224 This overlay allows for alternate rows of pixels to be 225 displaced through an angle, such that they are visible to 226 only 1 eye or the other without affecting contrast linearity. 227 The resolution of the overlay was 43 lenses per inch. The 228

Clinical Research Hess et al

Right eye view



Left eye view



Alignment procedure for the iPod. When the left and right eye Figure 1 views are of evenly colored squares of different color in the 2 eyes, the alignment is correct.

lenticular overlay and the software driver were supplied by 260 [Q7] Spatial View Inc.

To maintain the correct viewing angle for dichoptic stimulation, we keep the iPod display on a fixed stand, and the participants use a chin rest to ensure the viewing position does not change over the duration of the test. To control the game, players use a remote keyboard from a local computer connected wirelessly to the iPod. The on-screen touch buttons can also be used to play the game, although it is more convenient to use the keyboard with the iPod being kept stationary during a test. We are currently developing a number of refinements that will support real-time auto alignment of the display and allow for a relaxed game-playing posture when the device is held in the hands.

Game content

The game information is sent to the 2 eyes at different contrasts. In addition, block visibility belongs to one of 3 categories: 1) high-contrast blocks that are only visible to the amblyopic eye and not seen by the fellow eye, 2) low-contrast blocks that are only visible to the fellow eye and not seen by the amblyopic eye, and 3) binocular blocks that are visible to both eyes, in which the amblyopic eye sees the high-contrast version and the fellow eye sees the low-contrast version.

We experimented with 2 variations in the division of game content across the eyes. In the first approach, the falling Tetris is presented only to the amblyopic eye. The "grounded" blocks at the bottom of the game board consist of 2 types of block. The lower layer is visible to both eyes, in high contrast to amblyopic eye and low contrast in the fellow eye. The upper layer blocks, in low contrast, are presented only to the fellow fixing (nonamblyopic) eye. To play the game effectively in this setup, both eyes must be engaged in viewing and processing the game information. The amblyopic eye needs to follow the movement of the falling Tetris, whereas the fellow eye must register the formation of the grounded blocks to score a match. This is illustrated in Figure 2, where the fixing and amblyopic eve views are shown for the dichoptic presentation.

In the second approach, the grounded layer is seen by both eyes. The falling Tetris, on the other hand, is divided so that its whole shape is only seen if both eyes combine the information together. As each Tetris piece is made up of 4 blocks, we rendered 1 block visible to the amblyopic eye, 1 block to the fellow eye, and the remaining 2 blocks to both eyes.

Fixing eye view



Amblyopic eye view



Figure 2 Illustration of the fixing and amblyopic eye views of the dichoptically presented Tetris game in which the falling elements are seen by 1 eye and the upper layer of the ground elements by the other (the lower layer of the ground elements are seen binocularly). The contrast of the view seen by the fixing eye is reduced for each subject to a level that enables the game to be successfully played; it is then gradually changed over time until both eyes see the same contrast.

web 4C/FPO

∞

print ,

ARTICLE IN PRESS

Optometry, Vol 🔳, No 🔳, 🔳 2012

400

401

402

403

404

405

406

407

408

409

410

411

412

413

414

415

416

417

418

419

420

421

422

423

424

425

426

427

428

429

430

431

It should be noted that for both approaches, rather than
having an exclusive content division across the eyes, we
deliberately keep a number of binocularly visible blocks.
This binocular portion helps to bridge the spatial alignment
between various game elements, which might have otherwise appeared as misaligned if combined from two
disjointed monocular views with no shared elements.

351 352 **Subjects**

373

374

353 Ten participants with amblyopia were tested. All partici-354 pants were optically corrected and prismatically aligned 355 with prisms where necessary. All participants had normal 356 retinal correspondence. Inclusion criteria were a history or 357 identification of a cause for amblyopia, amblyopic eye 358 vision of 20/40 or worse with 20/20 or better in the fellow 359 eye associated with deficient or absent binocular function, 360 no history of current ocular pathology, and no other health 361 conditions that could influence training outcomes. The 362 clinical details of the amblyopes are given in Table 1. 363 All procedures were approved by the institutional ethics 364 committees, and all study protocols conformed to the 365 Declaration of Helsinki. All subjects wore optimal correc-366 tion for the testing distance of 50 cm (including a near 367 addition where appropriate). Ocular parameters were 368 [Q8] measured (using an IOL master version 3.01) on a subgroup 369 of anisometropic participants to determine if the anisome-370 tropia was axial or refractive in nature. Where the anisome-371 tropia was primarily axial (2 of 4 cases; subjects 9 and 10), 372

refractive correction was made up in a trial frame. In the 2 cases in which anisometropia was mixed (subjects 6 and 8), contact lenses were fitted during training to reduce aniseikonia and promote fusion. The subjects whose vision was corrected for the first time only wore their corrections during training because they found it difficult to tolerate the full prescription on a full-time basis. Visual acuity was measured at distance, using a LogMAR chart with Snellen crowded optotypes. Stereo acuity was measured at near use RanDot stereograms with full optical correction in place.

Statistical analysis

The Wilcoxon matched pair signed rank test was used to assess changes from pre- to posttraining in 1) the contrast ratio required for game play, 2) visual acuity in the amblyopic eye, and 3) stereo sensitivity. The relationships between the duration of training and training-related changes in the contrast ratio required for game play, visual acuity in the amblyopic eye, and stereo sensitivity were quantified using Spearman's rho. Finally, the independent samples Mann Whitney U test was used to compare training-related changes in contrast ratio, amblyopic eye visual acuity, and stereo sensitivity between the group of participants who were already fully refractively adapted before training and those who wore their correct refraction only during training. Nonparametric statistics were selected because of the small number of participants and the fact that the stereo sensitivity data did not meet the assumptions

ID	Age	Туре	Refraction	Visual acuity (LogMAR)	Squint	History
1	35	RE mixed	$+4.00/-1.50 \times 100$	0.7	ET Int 15°	Detected age 3 y, no patching or surgery, Rx prescribed at age 4
		LE	pl	0		
2	44	RE	-0.50-0.75 imes 115	0	Ortho	First detected at 6 y, no therapy, Rx never prescribed
		LE aniso	+7.00-2.50 imes 50	0.6		
3	17	RE	+1.25 DS	0	Ortho	Detected age 10 y, no patching, no surgery
		LE aniso	+5.25 DS	0.3		
4	32	RE	+0.75 DS	0	$XT \ 10^{\circ}$	Squint detected and Rx prescribed at age 4
		LE mixed	+4.00/-0.75 imes 005	0.9		
5	25	RE	+0.75	0	2° ET	Detected at age 5 y, patching, Rx prescribed
		LE mixed	+6.50/-1.75 imes 40	0.5		
6	51	RE	pl	-0.1	Ortho	First detected at 18 y, no therapy, full Rx never prescribed
		LE aniso	+3.00 DS	0.32		
7	23	RE	pl	0	ET 2°	Detected at 2 y, surgery at 5 y, patching, Rx never prescribed
		LE strab	+0.75/-1.25 imes 033	0.32		
8	40	RE	pl	-0.1	Ortho	First detected at 4 y, patching, Rx never prescribed
		LE aniso	+5.50/-1.00 imes 180	0.42		
9	23	RE	+0.25/-0.50 imes 180	-0.1	ET 3°	First detected at 2 y, surgery at 7 y, patching, full Rx never prescribed
		LE mixed	+2.25/-1.50 imes 110	0.3		
10	48	RE aniso	+2.50/-1.00 imes 80	0.46	Ortho	First detected at 5 y, patching, Rx never prescribed
		LE	pl	-0.1		
-		LE	pl	-0.1		r sphere; ortho = no ocular deviation; ET = constant esotre

514

515

516

517

518

519

520

521

522

523

524

525

526

527

528

529

530

531

532

533

534

535

536

537

538

539

540

541

542

543

544

545

546

547

548

549

550

551

552

553

554

555

556

557

558

559

560

561

562

563

564

565

566

567

568

569

570

457 for a parametric test, as not all participants had measureable458 stereopsis.

460 **Results**

459

496

497

498

499

500

501

502

503

504

505

506

507

508

509

462 To select the appropriate contrast level to display to the 463 fixing eye (the contrast was fixed at either 70% or 100% for 464 the amblyopic eye depending on the game type being used), 465 we used our abbreviated motion coherence technique⁵ in 466 which the contrast of the motion noise seen by the fixing eye is adjusted until a coherence threshold is achieved com-467 468 parable with that found for a normal eye. This gives the 469 contrast of stimuli seen by the fixing eye that allows binoc-470 ular combination to take place. For each subject we began 471 the game at this contrast level for the fixing eye. The game 472 was played for between 0.5 and 2 hours per session for 1 to 473 9 weeks. The frequency of sessions varied across partici-474 pants (see below). Over this time, the contrast presented 475 to the fixing eye was gradually increased. Our arbitrary 476 rule was to increase the fixing eye contrast only when stable 477 performance had been reached. Each adjustment was 478 between 10% and 20%. There were 2 indices of game 479 performance: falling speed (indicated by game level) and 480 score. These were used along with the subject's own 481 impressions as to whether the game can be successfully 482 played dichoptically.

483 Figures 3 through 5 show the training results for 10 484 amblyopic (5 anisometropic, 2 strabismic, and 3 anisome-485 tropic and strabismic) subjects at 3 training sites; Depart-486 ment of Ophthalmology, McGill University (subjects 1, 2, 487 3, 4), School of Optometry, University of Waterloo (subject 488 5), and Department of Optometry and Vision Science, 489 University of Auckland (subjects 6, 7, 8, 9, 10). Figure 3 490 shows the change in the interocular contrast ratio (fellow 491 eye contrast/amblyopic eye contrast) required for game 492 play pre- versus posttraining. A ratio of unity signifies 493 that the 2 eyes were able to do the task only at equal 494 contrasts, a value below unity signifies that the contrast 495

needed to be reduced for the fixing eye so that binocular combination could take place (i.e., a degree of suppression was present). In 5 (subjects 1, 2, 5, 9, and 10) of the 10 cases, the initial suppression was totally eliminated over the period of training. In another 4 cases, the degree of suppression was reduced over this same period (subjects 4, 6, 7, and 8). The final participant (subject 3) showed no effect of suppression on game play before training but was trained because there was no measurable stereopsis for this participant. There was a significant reduction in the required interocular contrast ratio between the eyes (i.e., a reduction in suppression) because of training for this group of 10 participants (Z = 2.67, P = 0.008). Importantly, in addition to these changes in interocular contrast ratio, we also found significant changes in both amblyopic visual acuity (see Figure 4) and stereo sensitivity (see Figure 5) for our group of adult participants with amblyopia. Nine of 10 participants showed improvements in amblyopic eye visual acuity (mean improvement, 0.19 Log MAR; standard error, 0.17), and this improvement was significant for the group (Z = 2.67, P = 0.008). Similarly, 6 of 10 participants showed an improvement in stereo sensitivity (see Figure 6), an effect that was also significant for the group (Z = 2.20, P = 0.028). Particularly noteworthy are subjects 1, 7, 9, and 10, who went from no measurable stereopsis to measureable stereopsis.

According to the availability of participants, 2 different training strategies emerged during the study. Subjects 1, 2, 3, 4, 5, and 7 played intensively for 1 to 3 hours per day for 2 to 3 weeks. Subjects 6, 8, 9, and 10, on the other hand, played between 30 and 45 minutes at each session and trained intermittently over a period of up to 9 weeks. Accordingly, we investigated whether the improvements we found in the interocular contrast ratio required for game play, amblyopic eye visual acuity, and stereo sensitivity were related to the number of training sessions, the number of hours of training per week, or the total number of training hours. Improvements in contrast ratio and

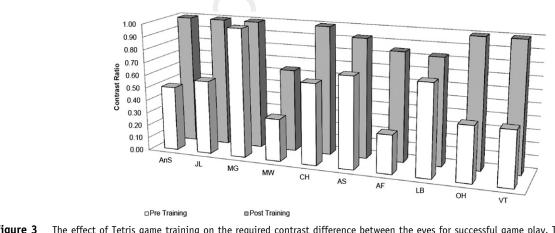


Figure 3 The effect of Tetris game training on the required contrast difference between the eyes for successful game play. The difference in contrast between the 2 eyes is shown as a contrast ratio (contrast to the fellow eye divided by contrast to amblyopic eye) and does not have an associated error, as this value was based on successful game play. Larger contrast ratios indicate less required contrast difference between the eyes and therefore less suppression. A contrast ratio of 1 indicates that that game could be played with identical contrasts seen by each eye, indicating an absence of suppression. Data are shown for game play pretraining and posttraining for each participant.

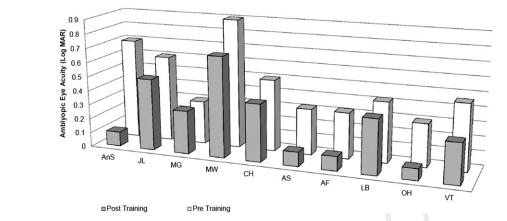


Figure 4 The effect of Tetris game training on amblyopic eye acuity (LogMAR). Data are shown for pretraining and posttraining measurements for each participant.

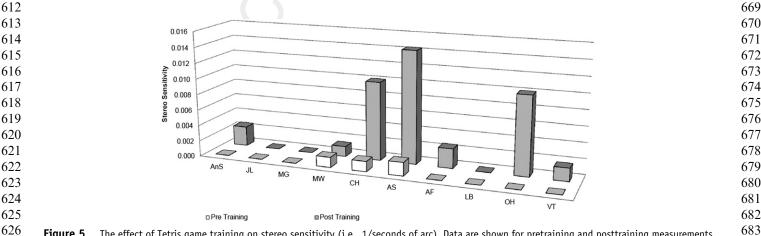
amblyopic eye acuity (LogMAR) were quantified as a percentage of change from pre- to posttraining. Because a reduction in suppression led to an increase in the contrast ratio (i.e., the ratio moved closer to 1), the percentage of improvement was calculated as (posttraining ratio - pre training ratio)/posttraining ratio. Conversely, an improve-ment in LogMAR acuity led to a reduction in the Log MAR value and, therefore, the percentage of improvement was calculated as (pretraining acuity - posttraining acuity)/ pretraining acuity. Because stereo sensitivity contained zero values, we quantified the improvement as posttraining stereo sensitivity - pretraining stereo sensitivity. We found a significant relationship between the total number of training sessions (mean, 15; max, 20; min, 10; standard deviation, 4) and improvements in contrast ratio (rho = 0.87, P = 0.001) 602 [Q9] and amblyopic eye acuity (rho = 0.80, P - 0.006), but not stereo sensitivity (P > 0.05). We did not find reliable correc-tions between hours of training per week or total hours of training and any of our outcome measures. This suggests that it was the repetitive exposure of the amblyopic visual system to contrast balanced stimuli that was important for this particular training approach. We also found a reliable relationship between the reduction in interocular contrast ratio and the improvement in amblyopic eye visual acuity (rho = -0.69, P = 0.026, see Figure 6), providing further

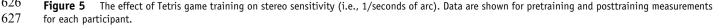
evidence for the link between reduced suppression and improved monocular function. In addition, we found that the improvement in amblyopic eye acuity was reliably related to the improvement in stereo sensitivity with larger improvements in acuity being associated with larger improvements in stereo sensitivity (rho = 0.71, P = 0.02, see Figure 7).

Participants 6, 8, 9, and 10 were followed up 1 to 2 months after training ceased. For the 3 participants who showed improvements in amblyopic eye acuity and stereopsis (subjects 6, 9, and 10), these improvements were still present at follow-up. One subject (subject 6) showed a 1-line improvement in amblyopic eye acuity at follow-up that was probably caused by wearing full refractive correction after training was completed. Based on this, we compared all the outcome measures between the group of participants who were fully refractively adapted (subjects 1, 4, 3, and 5) and those who wore their refractive correction for the first time only during training. There were no reliable differences. This issue is discussed further below.

Additional outcome measures

No adverse outcomes, such as diplopia or disturbed visual function, were found in this study. This is consistent with our previous work using a similar technique in the





Hess et al Clinical Research

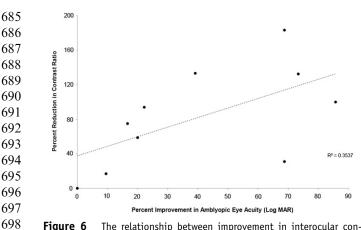
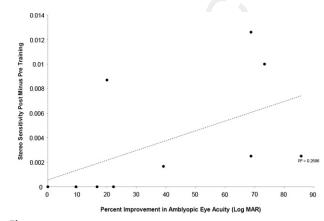


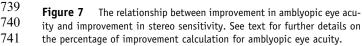
 Figure 6 The relationship between improvement in interocular contrast ratio and improvement in amblyopic eye acuity. See text for further details on the percentage of improvement calculations.

laboratory,^{2,3} where no cases of diplopia occurred.
However, diplopia remains an important consideration. A
number of participants reported positively on the nature
of training and portability and convenience of the device.
A group of participants also reported on feeling as though
their vision improved during the training period.

Discussion

A new platform for antisuppression treatment is described, which consists of a handheld device running a video game. This method, based on previous laboratory findings,²⁻⁴ allows controlled presentation of dichoptic stimuli of differ-ent interocular contrast within the context of an engaging video game, attractive to the younger age group to which this treatment is ideally directed. Conditions are arranged to provide (and to objectively verify) binocular stimulation within the gaming environment by manipulation of the contrast of elements seen by the fixing eye. Over time, these artificial viewing conditions where the eyes see stim-uli of different contrasts are slowly varied to more natural viewing conditions where the 2 eyes see stimuli of the same contrast, at which point binocular fusion under natural viewing conditions has been restored.





We show results for 9 of 10 subjects in which the degree of suppression, as quantified by the interocular contrast that could be tolerated under conditions of binocular combination, reduced over a period as short as 2 weeks by engaging in 1 to 3 hours of play per day. Lower levels of play per day and more sporadic training still resulted in reduced contrast imbalance if completed over a longer period. The 1 participant who did not improve (subject 3) showed no contrastbased suppression deficit before training. Consistent with previous studies using laboratory-based equipment,²⁻⁴ reducing suppression also often resulted in improved amblyopic eye visual acuity and stereopsis. In 9 of 10 cases, visual acuity improved because of training. In addition, in 6 of 10 cases, there was improved stereopsis, with some participants gaining stereopsis that was previously not detectable through clinical testing (subjects 1, 7, 9, and 10). In a subset of cases (4 of 10) that were followed-up, the improvement in visual function was still retained 1 to 2 months after the cessation of training. The sample size used in this pilot study is not sufficient for us to provide a clear profile for participants who did and did not respond; however, it is evident that not all participants responded in the same way. This is to be expected from a clinical population of adults with amblyopia. It is notable, however, that a significant improvement was found at the group level for this sample of adults with amblyopia.

This combination of antisuppression therapy with a portable video game platform provides an attractive alternative, or addition, to part-time patching as a treatment for amblyopia. The approach allows both eyes to be used in a period of enjoyable, yet attentive, play that is primarily directed at improving binocular vision with a secondary aim of reducing amblyopia. The fact that the treatment can be done with a handheld device makes it as convenient as patching but without the associated psychosocial side effects that often limit compliance with patching.^{6,7} In addition, our approach differs from patching in that the emphasis is on restoring binocular function rather than simply improving the monocular acuity of the amblyopic eye.

Refractive adaptation

Our results cannot be explained in terms of refractive adaptation. Our subjects can be divided into 2 groups, those who had adapted refractively (4 of 10) and those who were wearing spectacles for the first time (6 of 10). There was no statistical difference between any of the outcome measures for these 2 groups, showing that refractive adaptation has an insignificant influence. The reason for this is simply because of the differences in the time scales of refractive adaptation compared with our binocular therapy. All the available evidence^{6,8} clearly shows that refractive adaptation takes between 17 and 30 weeks of full day wear (approximately 1,000 hours). Our subjects were trained for between 6 and 36 hours in total. For the 6 subjects who did not habitually wear a correction, the correction was only worn during training. In addition, for one of these

ARTICLE IN PRESS

Optometry, Vol 🔳, No 🔳, 🔳 2012

856

857

858

859

860

861

862

863

864

865

866

867

868

869

870

871

872

873

874

875

876

877

878

879

880

881

882

883

884

885

886

887

888

889

890

891

892

893

894

895

896

897

898

899

900

901

902

903

904

905

906

907

908

799 subjects (subject 7), there was only a minimal refractive 800 error in the amblyopic eye. The influence of refractive 801 adaptation is not significant after 5 to 6 weeks (the mini-802 mum follow-up time in Pediatric Eye Disease Investigator Group and Monitored Occlusion Treatment of Amblyopia 803 Studies).^{6,8} Even this short period amounts to 400 hours 804 805 of spectacle wear, an order of magnitude longer than the 806 time our subjects wore their spectacles during training. 807

808 809 Relationship to previous work

810 A number of recent studies have shown that the monocular 811 function of adult amblyopes can be improved using 812 monocular⁹⁻¹² and binocular¹³ training procedures. It is 813 important to note that none of these methods, even the 814 dichoptic approach suggested by Cleary et al.,¹³ are 815 designed to improve binocular fusion, but instead they are 816 designed to improve the monocular function of the ambly-817 opic eye. Cleary et al.¹³ used dichoptic stimulation as a way 818 of engaging the amblyopic eye, as their primary aim was to 819 improve its acuity. Binocular training in amblyopia is not 820 new and has a long history that was well established 821 when the major amblyoscope (synoptophore) was in 822 common use. A number of studies have advocated this 823 approach, particularly if some level of fusion is 824 present.¹⁴⁻¹⁶ Our approach differs in that we manipulate 825 the interocular contrast (not the luminance as was used in 826 the amblyoscope), specifically to set up conditions in which 827 the information from the 2 eyes is combined. Furthermore, 828 we do this even when there is strong suppression without 829 any obvious binocular function. Our primary aim is to 830 improve binocular function, including fusion and stereop-831 sis. Any improvements in monocular acuity are a secondary 832 benefit. The majority of previous studies on amblyopia 833 treatment have used patching and assessed its duration 834 dependence. It is difficult to compare our approach with 835 conventional patching for a number of reasons. First, patch-836 ing is targeting monocular function, whereas our approach 837 targets binocular function. Second, there is no reason to 838 expect similar dynamics. Indeed, our current data suggest 839 a much shorter dose-response relationship compared with 840 occlusion therapy (36 hours as opposed to 400 hours⁸). 841 Third, occlusion therapy is not typically effective above 842 the age of about 10 years,⁸ whereas the current technique 843 is effective even for middle-age adults. 844

845

846 Future improvements847

Currently, we rely on the alignment being maintained for
the duration of the game using our initial alignment
procedure. Future methods will involve the use of a frontfacing camera to track eye position and to correct image
position in real time to ensure correct alignment and, hence,

- 853 854
- 855

accurate dichoptic presentation. There is no reason why the day-to-day improvement in performance cannot result in automatic adjustment to the interocular contrast, such that there will not be a need to make continual visits to the eye care specialist. The treatment history in terms of the game score and how contrast was adjusted over time during the out of office treatment could be available to the eye care specialist online so that professional monitoring, albeit remote, can continue throughout the treatment course without the need for continual visits.

Acknowledgments

We are most grateful to Spatial View Inc for providing the lenticular overlay material and the open GL software driver.

References

- Stewart CE, Fielder AR, Stephens DA, et al. Treatment of unilateral amblyopia: factors influencing visual outcome. *Invest Ophthalmol Vis Sci* 2005;46:3152-60.
- 2. Hess RF, Mansouri B, Thompson B. A new binocular approach to the treatment of Amblyopia in adults well beyond the critical period of visual development. *Rest Neurol Neurosci* 2010;28:1-10.
- 3. Hess RF, Mansouri B, Thompson B. A binocular approach to treating amblyopia: anti-suppression therapy. *Optom Vis Sci* 2010;87:697-704.
- 4. Mansouri B, Thompson B, Hess RF. Measurement of suprathreshold binocular interactions in amblyopia. *Vis Res* 2008;48:2775-84.
- 5. Black J, Maehara G, Thompson B, et al. A compact clinical instrument for quantifying suppression. *Optom Vis Sci* 2011;88:334-42.
- 6. Scheiman MM, Hertle RW, Beck RW, et al; for the Pediatric Eye Disease Investigator Group. Randomized trial of treatment of amblyopia in children aged 7 to 17. *Arch Ophthalmol* 2005;123:437-47.
- 7. Searle A, Norman P, Harrad R, et al. Psychosocial and clinical determinants of compliance with occlusion therapy for amblyopic children. *Eye* 2002;16:150-5.
- Stewart CE, Moseley MJ, Stephens DA, et al. Treatment dose-response in amblyopia therapy: the Monitored Occlusion Treatment of Amblyopia Study (MOTAS). *Invest Ophthalmol Vis Sci* 2004;45:3048-54.
- 9. Huang CB, Zhou Y, Lu ZL. Broad bandwidth of perceptual learning in the visual system of adults with anisometropic amblyopia. *Proc Natl Acad Sci U S A* 2008;105:4068-73.
- 10. Levi DM, Polat U. Neural plasticity in adults with amblyopia. *Proc Natl Acad Sci U S A* 1996;93:6830-4.
- Polat U, Ma-Naim T, Belkint M, et al. Improving vision in adult amblyopia by perceptual learning. *Proc Natl Acad Sci U S A* 2004;101: 6692-7.
- 12. Webb BS, McGraw PV, Levi DM. Learning with a lazy eye: a potential treatment for amblyopia. *Br J Ophthalmol* 2006;90:518.
- Cleary M, Moody AD, Buchanan A, et al. Assessment of a computer-based treatment for older amblyopes: the Glasgow Pilot Study. *Eye* 2009;23:124-31.
- 14. Ciuffreda KJ, Levi DM, Selenow A. *Amblyopia: basic and clinical aspects*. Boston: Butterworth-Heinemann; 1991:459.
- 15. Press LJ. Electronic games and strabismus therapy. *J Optom Vis Dev* 1981;12:35-9.
- 16. Schapero M. Amblyopia. Philadelphia: Chilton; 1971:253-4.
- 909 910 911
- 912

Our reference: OPTM 1146

AUTHOR QUERY FORM

	Journal: OPTM	
ELSEVIER	Article Number: 1146	

Dear Author,

Please check your proof carefully and mark all corrections at the appropriate place in the proof (e.g., by using on-screen annotation in the PDF file) or compile them in a separate list. Note: if you opt to annotate the file with software other than Adobe Reader then please also highlight the appropriate place in the PDF file. To ensure fast publication of your paper please return your corrections within 48 hours.

For correction or revision of any artwork, please consult http://www.elsevier.com/artworkinstructions.

Any queries or remarks that have arisen during the processing of your manuscript are listed below and highlighted by flags in the proof.

Location in article	Query / Remark: Click on the Q link to find the query's location in text Please insert your reply or correction at the corresponding line in the proof			
Q1	Please provide academic degree of "P. Zhang" author			
Q2	Please provide manufacturer city and state for Apple.			
Q3	Please provide manufacturer city and state location for Apple.			
Q4	Please verify that heading levels are set as intended, ie, primary, secondary, etc.			
Q5	Please verify unit of measure cd/m^2.			
Q6	Please provide manufacturer and manufacturer location for software and iPhone.			
Q7	Please provide city and state location for Spatial View Inc.			
Q8	Is IOL master version 3.01 a brand name? If so, please provide manufacturer information.			
Q9	In sentence starting We found a significant relationship" please confirm $P - 0.006$. Did you mean equals here?			
Q10	Please confirm that given names and surnames have been identified correctly.			

Thank you for your assistance.