An iPod treatment for amblyopia: An updated binocular approach

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KEYWORDS
Suppression; Amblyopia; Strabismus; Binocular vision

Abstract
We describe the successful translation of computerized and space-consuming laboratory equipment for the treatment of suppression to a small handheld iPod device. A portable and easily obtainable Apple iPod display, using current video technology offers an ideal solution for the clinical treatment of suppression. The following is a description of the iPod device and illustrates how a video game has been adapted to provide the appropriate stimulation to implement our recent antisuppression 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.

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 follows as a consequence of this. If this is correct, it is the binocular function that should be corrected first with the assumption 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 amblyopia.2-4 This work has also shown that understanding and measuring 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 structurally 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 systematically reduced with training under conditions that ensure the combination of information between the 2 eyes of an amblyopic observer.3 This simple antisuppression training

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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.²³

Initially, we used a laboratory approach with computer screens and a mirror haploscope and time-consuming but rigorous psychophysical measuring procedures.⁴ This led to the development of a compact head-mounted display where organic light-emitting diode screens mounted before each eye provided controlled, convenient dichotic stimulation and a more abbreviated testing procedure.³ We have now taken this a stage further and implemented our measurement and treatment regime on a handheld Apple iPod device.

Such a device can be used without any other viewing apparatus to measure the degree of suppression in a strabismic or anisometropic amblyopia and to provide the type of stimulation environment needed to restore binocular function as well as a degree of monocular function in amblyopic individuals. Because the device is portable and pocket size, it can be conveniently used outside the clinic. To enhance its appeal and acceptability with the younger age group, where the treatment will be most effective, we have implemented the training procedure as a Tetris video game.

**Rationale**

We have previously shown, using random dot stimuli and a dichoptic motion task, that information is combined between the 2 eyes of an amblyope when the contrast of the signal seen by the fixing eye is sufficiently reduced compared with that seen by the amblyopic eye.⁴ This, we argue, is because the suppressive drive from the fixing eye is contrast dependent. Furthermore, we have shown that prolonged viewing under these artificial conditions, in which the fixing eye contrast is reduced, leads to a strengthening of binocular vision in strabismic amblyopes, which is reflected in eventually being able to combine interocular signals of equal contrast.⁵ In our video game platform, we constructed a stimulus composed of elements seen by one or the other eye (i.e., a dichotic Tetris stimulus), and ensured that the game could only be played successfully if the information from the 2 eyes was combined (i.e., ensuring that there was binocular combination or fusion). We achieved this by reducing the contrast of the elements seen by the fixing eye, which, in turn, reduced the suppression of the amblyopic eye. Over time, if the game is played successfully, the contrast of the elements seen by the fixing eye can be increased with the aim of eventually eliminating the contrast offset between the eyes so that binocular combination can take place under unaided natural viewing conditions.

**Methods**

**System implementation**

**Display calibration and settings.** We used a second-generation iPod with its screen brightness set to about half the maximum level, at approximately 150 cd/m², with autobrightness turned off. The iPod screen has a resolution of 480 × 320. The game information is presented in grayscale 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, \(y \in [0, 255]\) is the pixel value assigned to all channels, and \(\gamma\) represents the display nonlinearity. To estimate \(\gamma\), 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 \(L_{foreground}\) is the luminance of the game block, and the background luminance \(L_{background} = L_{max} / 2\). 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 OpenGL using the iPhone software development kit. Each game screen sends 2 independent pictures simultaneously to the eyes. The 2 stimuli are combined into 1 interlaced image at the level of the display and are then redistributed to each eye separately via the lenticular screen overlay. This overlay allows for alternate rows of pixels to be displaced through an angle, such that they are visible to only 1 eye or the other without affecting contrast linearity. The resolution of the overlay was 43 lenses per inch. The...
lenticular overlay and the software driver were supplied by 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 eye 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.
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.

**Subjects**

Ten participants with amblyopia were tested. All participants were optically corrected and prismatic alignment with prisms where necessary. All participants had normal retinal correspondence. Inclusion criteria were a history or identification of a cause for amblyopia, amblyopic eye vision of 20/40 or worse with 20/20 or better in the fellow eye associated with deficient or absent binocular function, no history of current ocular pathology, and no other health conditions that could influence training outcomes. The clinical details of the amblyopes are given in Table 1. All procedures were approved by the institutional ethics committees, and all study protocols conformed to the Declaration of Helsinki. All subjects were optimal correction for the testing distance of 50 cm (including a near addition where appropriate). Ocular parameters were measured (using an IOL master version 3.01) on a subgroup of anisometropic participants to determine if the anisometropia was axial or refractive in nature. Where the anisometropia was primarily axial (2 of 4 cases; subjects 9 and 10), 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

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<td>35</td>
<td>RE mixed</td>
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<td>ET Int 15°</td>
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<tr>
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<td>RE</td>
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<tr>
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<td>Detected age 10 y, no patching, no surgery</td>
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<tr>
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<td>32</td>
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<td>+0.75 DS</td>
<td>0.3</td>
<td>XT 10°</td>
<td>Squint detected and Rx prescribed at age 4</td>
</tr>
<tr>
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<td>RE</td>
<td>+0.75 DS</td>
<td>0.9</td>
<td>2° ET</td>
<td>Detected at age 5 y, patching, Rx prescribed</td>
</tr>
<tr>
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<td>51</td>
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<td>-0.1</td>
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<td>First detected at 18 y, no therapy, full Rx never prescribed</td>
</tr>
<tr>
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<td>23</td>
<td>RE strab</td>
<td>+0.75/-1.25 × 033</td>
<td>0.32</td>
<td>ET 2°</td>
<td>Detected at 2 y, surgery at 5 y, patching, Rx never prescribed</td>
</tr>
<tr>
<td>8</td>
<td>40</td>
<td>RE aniso</td>
<td>+5.50/-1.00 × 180</td>
<td>-0.1</td>
<td>Ortho</td>
<td>First detected at 4 y, patching, Rx never prescribed</td>
</tr>
<tr>
<td>9</td>
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<td>+0.25/-0.50 × 180</td>
<td>-0.1</td>
<td>ET 3°</td>
<td>First detected at 2 y, surgery at 7 y, patching, full Rx never prescribed</td>
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<tr>
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<td>0.46</td>
<td>Ortho</td>
<td>First detected at 5 y, patching, Rx never prescribed</td>
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**Clinical details of participants tested**

ID = participant identifier; RE = right eye; LE = left eye; pl = plano; DS = diopter sphere; ortho = no ocular deviation; ET = constant esotropia; XT = constant esotropia; ET Int = intermittent esotropia; aniso = anisometropic; mixed = strabismic + anisometric.
for a parametric test, as not all participants had measurable stereopsis.

**Results**

To select the appropriate contrast level to display to the fixing eye (the contrast was fixed at either 70% or 100% for the amblyopic eye depending on the game type being used), we used our abbreviated motion coherence technique in which the contrast of the motion noise seen by the fixing eye is adjusted until a coherence threshold is achieved comparable with that found for a normal eye. This gives the contrast of stimuli seen by the fixing eye that allows binocular combination to take place. For each subject we began the game at this contrast level for the fixing eye. The game was played for between 0.5 and 2 hours per session for 1 to 9 weeks. The frequency of sessions varied across participants (see below). Over this time, the contrast presented to the fixing eye was gradually increased. Our arbitrary rule was to increase the fixing eye contrast only when stable performance had been reached. Each adjustment was between 10% and 20%. There were 2 indices of game performance: falling speed (indicated by game level) and score. These were used along with the subject’s own impressions as to whether the game can be successfully played dichoptically.

Figures 3 through 5 show the training results for 10 amblyopic (5 anisometropic, 2 strabismic, and 3 anisometropic and strabismic) subjects at 3 training sites; Department of Ophthalmology, McGill University (subjects 1, 2, 3, 4), School of Optometry, University of Waterloo (subject 5), and Department of Optometry and Vision Science, University of Auckland (subjects 6, 7, 8, 9, 10). Figure 3 shows the change in the interocular contrast ratio (fellow eye contrast/amblyopic eye contrast) required for game play pre- versus posttraining. A ratio of unity signifies that the 2 eyes were able to do the task only at equal contrasts, a value below unity signifies that the contrast 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 measurable 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
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 \((\text{posttraining ratio} - \text{pretraining ratio})/\text{posttraining ratio}\). Conversely, an improvement in LogMAR acuity led to a reduction in the Log MAR value and, therefore, the percentage of improvement was calculated as \((\text{pretraining acuity} - \text{posttraining acuity})/\text{pretraining acuity}\).

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 \((\rho = 0.87, P = 0.001)\) and amblyopic eye acuity \((\rho = 0.80, P = 0.006)\), but not stereo sensitivity \((P > 0.05)\). We did not find reliable corrections 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 \((\rho = -0.69, P = 0.026, \text{see Figure 6})\), 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 \((\rho = 0.71, P = 0.02, \text{see Figure 7})\).

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
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, 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 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, allows controlled presentation of dichoptic stimuli of different 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 stimuli 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 contrast-based suppression deficit before training. Consistent with previous studies using laboratory-based equipment, 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. 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 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
in the amblyopic eye. The influence of refractive adaptation is not significant after 5 to 6 weeks (the minimum follow-up time in Pediatric Eye Disease Investigator Group and Monitored Occlusion Treatment of Amblyopia Studies). Even this short period amounts to 400 hours of spectacle wear, an order of magnitude longer than the time our subjects wore their spectacles during training.

**Relationship to previous work**

A number of recent studies have shown that the monocular function of adult amblyopes can be improved using monocular and binocular training procedures. It is important to note that none of these methods, even the dichoptic approach suggested by Cleary et al., are designed to improve binocular function, but instead they are designed to improve the monocular function of the amblyopic eye. Cleary et al. used dichoptic stimulation as a way of engaging the amblyopic eye, as their primary aim was to improve its acuity. Binocular training in amblyopia is not new and has a long history that was well established when the major amblyoscope (synoptophore) was in common use. A number of studies have advocated this approach, particularly if some level of fusion is present. Our approach differs in that we manipulate the interocular contrast (not the luminance as was used in the amblyoscope), specifically to set up conditions in which the information from the 2 eyes is combined. Furthermore, we do this even when there is strong suppression without any obvious binocular function. Our primary aim is to improve binocular function, including fusion and stereopsis. Any improvements in monocular acuity are a secondary benefit. The majority of previous studies on amblyopia treatment have used patching and assessed its duration dependence. It is difficult to compare our approach with conventional patching for a number of reasons. First, patching is targeting monocular function, whereas our approach targets binocular function. Second, there is no reason to expect similar dynamics. Indeed, our current data suggest a much shorter dose-response relationship compared with occlusion therapy (36 hours as opposed to 400 hours). Third, occlusion therapy is not typically effective above the age of about 10 years, whereas the current technique is effective even for middle-age adults.

**Future improvements**

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 front-facing camera to track eye position and to correct image position in real time to ensure correct alignment and, hence, 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**

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**References**


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