A Game Platform for Treatment of Amblyopia

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***Abstract*—We have developed a prototype device for take-home use that can be used in the treatment of amblyopia. The therapeutic scenario we envision involves patients first visiting a clinic, where their vision parameters are assessed and suitable parameters are determined for therapy. Patients then proceed with the actual therapeutic treatment on their own, using our device, which consists of an Apple iPod Touch running a specially modified game application. Our rationale for choosing to develop the prototype around a game stems from multiple requirements that such an application satisfies. First, system operation must be sufficiently straightforward that ease-of-use is not an obstacle. Second, the application itself should be compelling and motivate use more so than a traditional therapeutic task if it is to be used regularly outside of the clinic. This is particularly relevant for children, as compliance is a major issue for current treatments of childhood amblyopia. However, despite the traditional opinion that treatment of amblyopia is only effective in children, our initial results add to the growing body of evidence that improvements in visual function can be achieved in adults with amblyopia.**

***Index Terms*—Biology, biomedical engineering, brain stimulation, cognition, cognitive informatics, cybernetics, medical diagnosis, medical treatment, neural engineering, physiology, psychology, psychometric testing, sensitivity and specificity.**

I. Introduction

AMBLYOPIA is a prevalent visual disorder, with an incidence of approximately 2% [1], [2], afflicting 6 million Americans, of which 300 000 are aged five years or less. It is characterized by impairment of function in the affected eye due to suppression by the normal, nonamblyopic eye. Importantly, this is not due to a defect with the eye itself but rather an abnormal development of the visual system at a cortical level where information first interacts between the two eyes. When both eyes are viewing, the input from the amblyopic eye has a greatly impoverished or absent contribution to visual perception. Therefore, under normal viewing conditions, an amblyopic individual with both eyes open will only see a monocular (single eye) representation of their visual environment. This leads to a number of perceptual problems, the most pronounced being impaired depth perception. It has been assumed that loss of visual function in one eye (i.e., amblyopia) is the primary problem and that loss of binocularity is a secondary consequence. However, an alternative possibility is that the loss of binocularity is the primary problem, which then leads to amblyopia. If this is so, then the current approach to therapy, which is to restore the vision in the amblyopic eye using only monocular methods, may not be ideal. A better approach may be to target binocular visual function directly.

Traditional treatments for amblyopia are limited to children under 12 years of age [3] and entail occlusion or blurring of vision in the good eye through the use of a patch or eye drops. Penalization of the good eye has numerous negative effects on children. They are forced to live with impaired vision, there are psychological effects of wearing an eye-patch [4], particularly at school and risks of reverse-amblyopia where the good eye becomes amblyopic [5]. Although penalization treatments are effective, they are plagued by compliance issues due to their aversive nature [6].

Penalization approaches have not been used for adults due to an assumed lack of sufficient plasticity in the visual system after initial development to allow for functional recovery of vision. However, recent studies have shown that the monocular function of adult amblyopes can be improved using monocular [7]–[10] and binocular (i.e., with two eyes open) [11] training. It is important to note that none of these methods, even the dichoptic approach suggested by Cleary *et al.* [11], are designed to improve binocular fusion, but instead 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. Our approach differs in that we manipulate the interocular contrast, specifically to set up conditions in which the information from the two eyes is combined. Our primary aim is to improve binocular function, including fusion and stereopsis. Any improvements in monocular acuity are a secondary benefit.

There is also recent evidence that the binocular function in amblyopic adults is not permanently lost [12], [13] and can also be improved through specialized behavioural training [14], [15]. This motivated our approach to the assessment and treatment of amblyopia, a disorder that has traditionally been viewed as a monocular problem. The alternative we present here is specifically designed to reduce suppression under conditions that actively promote binocular fusion.

Our approach shows strong promise in terms of its therapeutic effect and overcomes many of the problems described above, associated with conventional monocular patching therapy. The remainder of the paper is organized as follows. In Section II, we describe the underlying principles for our treatment method based on differential interocular contrasts. Next, in Section III,

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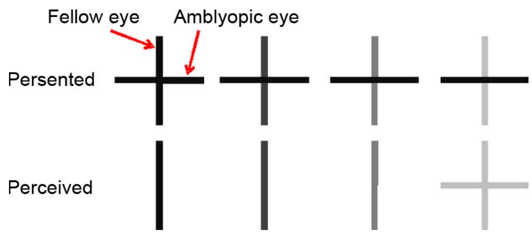
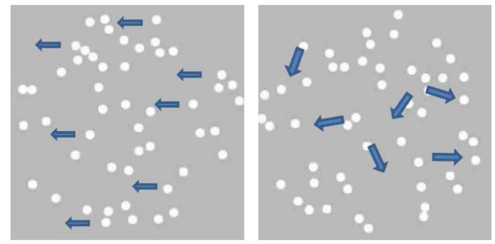


Fig. 1. A simplified schematic representation of the balancing procedure using contrast to balance the images of the two eyes in amblyopia. When two lines, one horizontal and one vertical are presented to each eye of a normal observer a cross is perceived as the lines are binocularly fused. This is not the case for an amblyope where, due to suppression, only the line presented to the fellow fixing (nonamblyopic) eye will be perceived (compare top row that shows the presented stimuli with the bottom row that shows the amblyope's percept). However, if information presented to the fellow eye is weakened (in this case the line is reduced in contrast) the amblyopic visual system can overcome the suppression and binocular vision can be achieved. The relative contrast between the eyes at this point is the "balance point" where suppression is no longer sufficiently strong to inhibit binocular combination.



(a) (b)

Fig. 2. Dot stimulus, with all signal dots moving in the same horizontal direction for the amblyopic eye (a) and noise dots moving in random directions for the fellow eye (b). To engage the amblyopic eye, the contrast ratio is set to the balance point where the signal dots have a higher contrast. (a) Signal. (b) Noise.

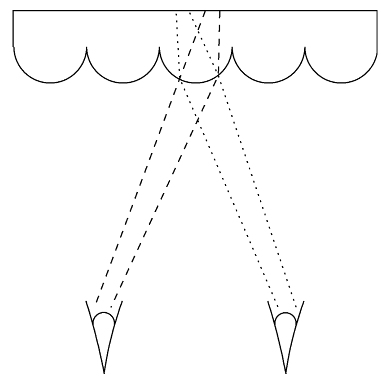


Fig. 3. Lenticular overlay renders separate images to the two eyes.

we describe the design requirements leading to the proposed game platform. In Section IV we cover the software and hardware used to create this treatment platform, followed by details of the game strategies used to deliver differential contrasts to the eyes. We then describe, in Section V, the experimental procedure adopted and briefly summarize results obtained from a multi-site trial that was conducted with two prototype devices, followed by our conclusions in Section VI.

II. An Alternative Contrast-Based Approach to Treatment of Amblyopia

Our approach to this problem was motivated by the observation that if visual stimuli are presented separately but simultaneously to each eye, in a manner that sufficiently favors the amblyopic eye (e.g., by reducing image contrast to the nonamblyopic eye), at a certain "balance point" of contrasts, both eyes contribute to visual perception [16]. Determining this balance point of contrasts is necessary for optimum cooperation between the eyes and hence, successful treatment [13]–[15].

Consider an extreme case when the contrast to the nonamblyopic, fellow fixing eye, henceforth, simply "fellow eye," is reduced all the way to zero and the contrast to the amblyopic eye is set at the maximum limit of the display. This is analogous to applying a patch over the good eye, thus channelling all incoming visual information through the weaker eye. In other words, the amblyopic eye would then dominate the visual system. However, if we gradually increase the contrast seen by the fellow eye towards the balance point threshold (Fig. 1), then it has been shown [16] that the brain combines information from the two eyes, shifting from a dominant-eye condition to an equilibrium where both eyes contribute to conscious visual perception. In amblyopes, a higher contrast must be presented to the amblyopic eye than to the fellow eye to maintain this equilibrium, otherwise, the subject will return to amblyopic viewing, i.e., suppressing the information received by the weaker eye. The higher this "contrast ratio," the greater the imbalance between the eyes.

The proposed method requires the subject to observe a visual stimulus presented dichoptically (separate images to each eye) at the balance-point contrast ratio for a period of time, then increases the difficulty of the task by slightly raising the fellow-eye contrast. This makes it possible, after sufficient treatment, to reach an equal-contrast viewing condition, as the subject continuously adapts to maintain binocular combination of the images presented to each eye as the contrast ratio decreases.

As the severity of amblyopia varies amongst subjects, it is necessary to establish the initial contrast ratio for each subject individually. The question, at the start of treatment, is how much to lower the contrast for the fellow eye so that the amblyopic eye will function equally well. This issue is resolved through the use of a task that requires the detection of a signal presented to one eye against noise presented to the other eye. Signal and noise are represented by two arrays of dots, where all the signal dots move in the same horizontal direction and the noise dots move in random directions (Fig. 2).

The observer's task is to identify the signal dot direction. Using a two-alternative forced choice response method, such an experiment requires minimum interaction by the observer, who is only responding to whether the stimulus movement is to the left or right. Task difficulty is manipulated by keeping the total number of dots constant but varying the proportion of signal dots (i.e., those moving in the same direction) relative to noise dots. The threshold number of signal dots required to identify the signal direction correctly is known as the motion coherence threshold [17], [18] and can be thought of as a signal/noise ratio. By presenting the signal dots to one eye and the noise dots to the other, it is possible to vary the contrast of the dots in the fellow eye until the motion coherence thresholds are the same, regardless of which eye sees the signal and which eye sees the noise

(a) (b)

Fig. 4. The game prototype using an iPod Touch with an overlay lenticular lens, which provides different content to each eye. The two pictures are presented simultaneously, but each is only visible to a specific horizontal viewing angle. (a) View to the fellow eye: All the information sent to the fellow eye is in low contrast. Static Tetris blocks buried below other blocks at the bottom of the gameboard are fully visible. (b) View to the amblyopic eye: All the information sent to the amblyopic eye is in high contrast. The falling Tetris is visible, as are some of the buried blocks at the bottom of the gameboard.

[16]. This is indicative of normal binocular function where both dot populations are contributing to conscious visual perception. The contrast ratio at which this occurs in an amblyope is considered to be the balance point.

Recent research has found that repetitive exposure to dichoptic stimuli (emphasizing either spatial or motion information) of this type resulted in an improvement in the combination of visual information between the eyes of amblyopes [14], [15], [19]. In a previous study using a laboratory method of dichoptic presentation (i.e., an eight-mirror haploscope) we reported improvements in binocular and monocular performance for ten strabismic amblyopes [15]. Our follow-up is limited to six months but in the cases that we have followed up, the improvements were sustained. Patient selection was limited to those with either straight eyes or small angle squints, all prismatically corrected during treatment. We have not had any cases of diplopia, probably because we actively promote binocular combination and sensory fusion during training. Whether the motor status has changed as a result of the sensory fusion is presently being investigated. Moreover, this new treatment was found to be effective in adult subjects. While current traditional treatments for amblyopia are only considered to be effective for children whose visual systems are still developing [3], our results are consistent with a number of previous studies demonstrating visual improvement in adults with amblyopia [7]–[11].

Whereas other treatments only deal with monocular loss and thus have a high relapse rate [20], our technique directly addresses the binocular suppression that underpins much of the visual loss in the amblyopic eye.

III. Design Considerations

From a design perspective, the underlying principle for the rehabilitation process is to exploit a contrast difference to coerce the two eyes into cooperating on a visual task. For reasons elaborated upon below, the simple dot stimuli are unsatisfying for long-term treatment. Instead, we adopted an implementation of a modified Tetris game on a mobile device for this purpose. The remainder of this section expands on these objectives, discussing how they are realized in our mobile treatment device.

A. *Mobility*

Since treatment of this form is likely to offer superior results with frequent exposure, scheduling considerations for the clinician, patients and parents (of children being treated) favour a solution that does not require administration in the office of a vision care practitioner. In order to deliver the treatment effectively, reach the maximum number of patients and compete with monocular approaches, a take-home device is imperative. In taking this balanced-contrast treatment outside the environment of a vision laboratory, we envision that the new platform should be compact and mobile, allowing users to carry it easily and use it at their convenience.

We are then faced with the question of how to send the different contrast images to each eye. Prior options included a CRT monitor with a view barrier between the two eyes and a less constraining head-mounted display. Similarly, polarized or shutter glasses technology, coupled with an appropriate screen display, were considered. However, these possibilities seemed less suitable for supporting mobile play, maximizing portability, gaining user acceptance of the technology and minimizing cost for the additional hardware.

Ideally, we wanted to avoid the need for special eyegear of any form. This motivated our adoption of display technology based on the characteristics of a lenticular array surface,[1] placed overtop of an LCD display[2] (Fig. 4). The lenticular sheet consists of a series of small cylindrical lenses, through which the underlying image is divided into interleaving stripes, visible at different viewing angles (Fig. 3). This principle, popularized in Cracker Jack prizes from the 1950s, results in the appearance of different images as either the display surface or the viewer changes angle. Because the viewer does not need to wear any special eyegear, the exercise is less strenuous over an extended period of use.

This technique may also be employed to achieve autostereoscopic displays, which provide stereographic (3D) effects to viewers without the requirement of special eyegear. In our case,

[1]Our implementation makes use of the 3DShell from Spatial View (http://www.spatialview.com).

[2]We have experimented with both a Sony VGN-UX280P Ultra-Mobile Personal Computer (UMPC) and the Apple iPod Touch.

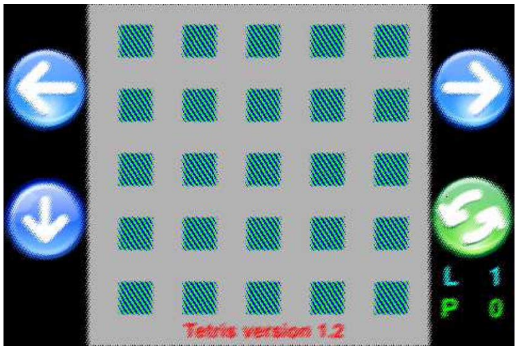


Fig. 5. Screen capture showing the calibration of information for the two eyes. The user must move the device back and forth and change the horizontal angle of the screen until they see only green squares in one eye and blue squares in the other. The lenticular overlay separates the information between the two eyes, but it must be correctly aligned with the surface of the display prior to use to prevent bleeding of information between the two eyes.

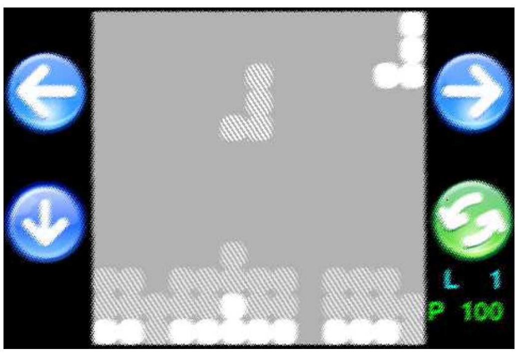


Fig. 6. Sample Tetris screenshot during a game, without the lenticular layer. Note the falling Tetris and top two blocks in each column at the bottom of the screen are striped such that the lenticular material sends the block to only one eye. In this example, the falling block is visible only to the amblyopic eye, whereas the striped blocks at the bottom of the screen are visible only to the fellow eye. The latter group is also dimmer, resulting in these blocks having lower contrast in order to engage the amblyopic eye.

stereopsis is not the intended (or at least, the primary) effect, but we can exploit the same technology to provide the appropriate differentiated presentation of information to the two eyes.

B. Ease of Setup

While special-purpose software and hardware can be used in a lab environment, use of the device should require zero-to-minimal setup effort.

Our hardware prototypes are self-contained systems that can easily be held in in the hands even during long sessions. No additional hardware such as special glasses or positioning mechanisms are required. The platform used in our experiments is an Apple iPod Touch device, which can be run on battery for many hours and is sufficiently light and small to be carried easily and used throughout the day as time permits, avoiding the need for scheduling specific times and locations for the therapy. One of the drawbacks of the iPod Touch, however, is that movement of either the display or the user's head can impair the effect of the lenticular overlay since it is highly dependent on viewing angle (Fig. 5). At an incorrect angle, there is significant bleeding of the image for the left eye into the right and vice-versa. With enough of a horizontal shift, the signals to the eyes may be swapped completely, thus negating any therapeutic effect. Other devices, such as the Sony UMPC used for our second handheld prototype, are significantly larger and heavier, but have an integrated front-facing camera that can be used to track the user's eye position relative to the screen. Using this information, the image behind the lenticular material can be adjusted to compensate for the user's changing head position relative to the screen, reducing or eliminating the problem of display bleeding between the two eyes.[3] Since front-facing cameras are an increasingly common option on handheld devices, we expect this to be a viable option for a future commercial system.

C. User Engagement

Although the dot stimulus on which the approach was first validated demonstrated initial success, we wanted to apply this to a more engaging and pleasant activity that would encourage usage and hence, reduce or eliminate the compliance issues noted above. For this reason, we were motivated to adopt a game as the visual task. Significantly, the game paradigm ensures that the user is more actively engaged as an interactive participant.

Inspired by a recent study showing that a prolonged period of Tetris playing can lead to changes in the temporal pole, a brain area that integrates visual information [21], we decided to adopt a modified Tetris game as the visual task. Interestingly, in normal subjects, action video games have been shown to improve a range of visual skills, but this does not occur for Tetris [22].

Tetris is a simple, popular game that is easy to learn. It requires a player to align various falling elementary shapes, which randomly appear one at a time at the top of the screen. The objective is to form complete rows of blocks as the pieces reach the bottom of the screen. While the previous dot-based experiment provides only two alternative forced choices (2AFC), left and right, Tetris players interact continuously with controls for rotating the falling blocks and shifting them left and right. Moreover, the block-based construction of game elements provides a convenient framework to customize the visibility and contrast on a block-by-block basis.

This task relies on the ability to see and combine the shape and orientation of the falling blocks with the gaps in the partially completed rows at the bottom of the screen. In addition, Tetris can be played by an amblyope as it does not require stereo vision. However, an amblyopic player would ordinarily perceive the game only through the fellow eye when both eyes are open. To elicit cooperation between the eyes, the graphical contents of our modified Tetris game (see Fig. 6) are partitioned into three groups as follows. Some content is sent to the amblyopic eye at high contrast, a second group is sent to the good eye at reduced contrast and a third set is sent to both eyes. The last of these groups is presented at high contrast to the amblyopic eye and at low contrast to the fellow eye according to the contrast ratio of the current game state.

[3]This tracking and compensation is implemented in the proprietary Spatial View SDK used to build the software for our prototypes.

IV. System Implementation

A. Screen Calibration and Contrast Presentation

The game is implemented completely in grayscale by setting the red, green and blue values of each pixel to be equal, effectively turning the iPod into an 8-bit grayscale device. The luminance of the iPod display is linearized using a grayscale calibration [23].

Contrast of a game element is defined by the relative luminance of a Tetris block against the uniform background of the gameboard and is calculated as follows:

$$C = \frac{L_{\text{tetris}} - L_{\text{background}}}{L_{\text{background}}}. \tag{1}$$

The background luminance is set to half of the maximum output luminance, i.e., $L_{\text{background}} = L_{\max}/2$, where $L_{\max}$ is the screen luminance where all pixels are set to 255. The foreground luminance is determined respectively from the contrast levels seen by the amblyopic and fellow eyes. The amblyopic-eye foreground luminance is kept at $L_{\max}$ to maintain the highest contrast. For the fellow eye, the contrast corresponding to the balance point is used to calculate the luminance, which varies between $L_{\text{background}}$ and $L_{\max}$.

B. Software

The game software is written in Objective-C using the iPhone software development kit. We use OpenGL (ES) for rendering and all game controls are handled inside the OpenGL drawing loop. The image processing technique to interlace the images sent to the two eyes into a single image for display on the iPod is provided by a proprietary rendering engine from Spatial View Inc.

Due to the nature of the lenticular overlay, if the user's head moves relative to the screen, or if the device moves during the experiment, the information intended for each eye may be sent partially to the opposite eye, resulting in crosstalk. The interference is minimal if the viewing angles are maintained properly during the game. For example, in Fig. 4, where the high-contrast tetris is intended only for the right view, its leakage onto the left view is barely visible.

To control this in our initial field test, the user's head was fixed in a chin rest to ensure that it did not change position as they played the game. In addition, instead of implementing the game's control buttons on the iPod's touchscreen, which would potentially result in the user moving the iPod when touching the controls, a wireless connection to another computer was used to allow remote control of the game through a standard keyboard.

In future prototypes and any commercial system, our intent would be to use either the touchscreen itself for game control, or find a device with built-in hardware gaming controls. Several factors encourage optimism that this will be possible, despite the increased difficulty a user will experience trying to maintain the correct head position and angle relative to the screen while also manipulating controls located on the device. First, the lenticular material has improved significantly, just within a one year time frame of our initial development, with a much greater tolerance for small shifts in viewing angle. At this point, we believe it is likely that a cooperative user who makes an effort to maintain the correct angle while playing, coupled with regular verification operations to ensure that the viewing angle is still correct, will achieve a therapeutic effect. Second, with the emergence of mobile devices such as the iPhone 4, with integrated front-facing cameras, it is now feasible to consider adding support for head-tracking of the user's position relative to the screen, without affecting the portability of the device. This would dramatically reduce the sensitivity to view angle, as the rendering engine can compensate for such changes. Third, we are exploring ways to provide visual indication, via the game itself, when the user goes off-axis, without requiring the user to close either eye. This would allow for self-correction by the player, without interrupting game play.

This third option is particularly interesting since it does not require any hardware changes or improved lenticular material. One possibility to generate the necessary feedback regarding screen angle relative to the player's head, without disturbing game play, is as follows. A border could be rendered around the edge of the screen, consisting of squares directed alternately to the left and right eye at the balance point contrast. When viewed by an amblyope in the correct head position relative to the screen, the border would appear continuous. However, as they move off-axis, the border would become a dashed line as the high contrast squares bleed over to the good eye and lower contrast squares to the weaker eye. Note, however, that as the balance point moves closer to equality between the two eyes, this mechanism gradually loses its effectiveness.

C. Game Strategies

The fundamental element of the Tetris game is a square block. Different shapes are formed with this building block and are sometimes referred to by the letter they resemble. Several game strategies were explored, with the goal of encouraging binocularity in order to gain a therapeutic effect through cooperation between the eyes.

1) Contrast Difference: Each square block on the gameboard belongs to one of three categories, classified according to its contrast and visibility. The block contrast is defined by the relationship between the block and the background luminance in (1). Visibility refers to whether a block is visible to the amblyopic eye only, the fellow eye only, or to both eyes. The three categories are as follows.

- High contrast blocks only visible to amblyopic eye.
- Low contrast blocks only visible to the fellow eye.
- Blocks visible to both eyes.

When starting the game for the first time, the contrast ratio value is determined empirically for each player using the dot stimulus method.

For our initial experiment, we presented blocks visible to both eyes at an identical level of contrast. However, we later realized that this approach risks having those blocks ignored by the amblyopic eye, in favor of the fellow eye. We therefore modified these binocular blocks so that maximum contrast is seen by the amblyopic eye, while the fellow-eye contrast is at a value just above the balance point. This should ensure that the amblyopic eye remains engaged, but with the blocks still easy to see and track with both eyes cooperating.

2) Game Scoring and Difficulty-Level Adjustment: Players may become disinterested in a computer game if it is not sufficiently challenging. For this reason, many games include a score display and dynamically adjust the difficulty level. In Tetris, a more difficult level typically means that the Tetris blocks fall faster. However, for our platform, because much of the game information is divided between two eyes, the difficulty does not depend solely on the speed factor; it is also affected by how well the eyes cooperate at a given contrast ratio. Thus, we can increase the game difficulty by decreasing the contrast ratio between the two eyes.

While either of the mechanisms above may be employed to vary game difficulty, the former is strictly beneficial as a means of maintaining player interest, while the latter optimizes potential therapeutic effects. To maintain player interest and at the same time achieve maximum therapeutic effect, we devised separate mechanisms for adjusting the game speed and contrast difference.

First, we consider adjustment of the block speed. In Tetris, the score is based on the number of rows of Tetris blocks that have been removed from the gameboard. When a predetermined number of rows have been removed, the game speed is increased to a higher level of difficulty. Speed is specified by the number of seconds it takes for a block to fall the space of one row. Starting from an initial falling time of 700 ms/row, we decrease this value by 50 ms every time the level advances. Eventually, the speed of the game may render it nearly impossible to play and any therapeutic effect is lost. To prevent this from happening, game performance is monitored continuously. When the player fails to score in three consecutive games, the algorithm automatically reduces the existing speed by 50 ms per line.

After determining the appropriate block speed, contrast needed to be adjusted to move the player toward a balanced-eye condition, which is the goal of the therapy. We did not have any prior data for this particular stimulus that might guide an automated inter-ocular contrast difference adjustment for maximal therapeutic benefit. Therefore, we opted for a manual approach in our initial experiment. Essentially, we wanted the experimenters to use their judgement to move aggressively toward equal contrast between the eyes, while ensuring that game performance remains stable. The initial contrast difference is set to reflect the balanced-contrast condition, as measured during the dot stimulus experiment. The operator then reviewed the player's game performance each day and based on consultation with the player, adjusted the contrast for the fellow eye upwards, thus moving closer to an equal-contrast condition and making the game more difficult for an amblyope to play.

For the remainder of this section, we elaborate on two different strategies we considered for dividing the presentation of game information between the eyes.

3) Game Strategy 1: Falling Tetris to One Eye, Ground Rows to the Other Eye: The falling Tetris (at high-contrast) is directed to the amblyopic eye, while the stationary blocks on the ground are divided into two groups (Fig. 7). The two top blocks of each column are rendered in low contrast and visible only to the fellow eye, while all remaining stationary blocks underneath are visible to both eyes in high contrast.

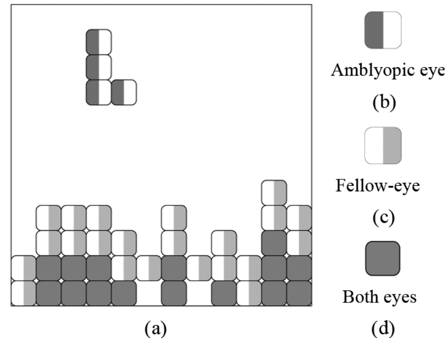


Fig. 7. Game strategy 1: (a) Tetris game; (b) high-contrast block visible only to amblyopic eye; (c) low-contrast block visible only to fellow eye; (d) all other blocks visible to both eyes in high contrast.

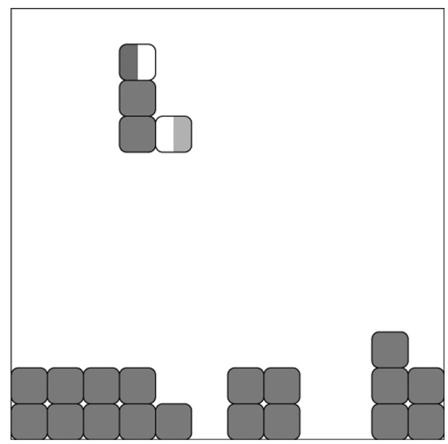


Fig. 8. Game strategy 2: Falling blocks split between the two eyes.

During play, the most relevant information comes from the shape of the falling Tetris and the pattern of the ground surface. Since this information is split between the two eyes, it must be combined to make the game playable. In addition to the shape information, the amblyopic eye has to track the Tetris' motion, while the presentation to the fellow eye remains stationary. This asymmetrical arrangement forces the amblyopic eye to work harder in the game, hopefully increasing any therapeutic effect.

4) Game Strategy 2: Falling Tetris Split Between Two Eyes, Ground Rows Presented Equally to Both Eyes: For the second strategy, each falling Tetris is split into three: one high-contrast section only visible to the amblyopic eye, one low-contrast section only visible to the good eye and a middle section visible to both (Fig. 8). All the stationary blocks on the game board are also visible to both eyes and presented in high contrast.

This arrangement forces both eyes to follow the Tetris movement in order to see the complete shape. The purpose of having the central blocks of each Tetris visible to both eyes is to provide the player with a fusion cue, which helps with binocular combination of the peripheral blocks that are only visible to a single eye. In an earlier prototype, we divided the Tetris into two halves with each half exclusively seen by only one eye. This design introduced a misalignment effect in the Tetris shape, which

TABLE I
PARTICIPANT'S DAILY GAME SCHEDULE

Time	Activity	Duration
10:10 am	Game learning (first-day only)	5 mins
SESSION 1		
10:15 am	Play game	15 mins
10:30 am	Pause game; subject takes a rest	3 mins
10:35 am	Continue playing	15 mins
10:50 am	Pause game; subject takes a rest	3 mins
10:55 am	Continue playing	15 mins
11:10 am	Session break	15 mins
REPEAT SESSION, if time permits		

TABLE II
OPERATOR'S MEASUREMENT SCHEDULE

Daily
• Measure balance point (dot-stimulus on iPod Touch) • Adjustment of the appropriate balance point for the Tetris game based on the experimenter's knowledge of their previous game performance, the measured balance point, and how aggressively the experimenter wants to move towards equal contrast between the eyes.
Every five-day (including first and last)
• Measure balance point using dot-stimulus on stereo goggles • Stereo and visual acuity, refractive and oculomotor status

was perceived by nonamblyopes even when the Tetris was stationary. The addition of the fusion block helped alleviate this problem.

V. Experiment Design and Evaluation

The user's degree of binocularity might also be inferred from the game scores directly, rather than by using a balance point measure such as the dot stimulus. However, as amblyopia is a visual disorder, a clinical assessment of the condition is preferred to establish and monitor its severity from the start of treatment and throughout the experiment. In any case, an independent measure of amblyopia and binocular status is useful at least in the initial trials, since we hope in the future to construct a self-adjusting game for rehabilitation through correlation between such data and game performance. Thus, to monitor progress in the current experiment, we interleave game sessions with regular measurements using the dot stimulus on the game device as well as more standard clinical tests for binocular fusion (Worth 4 dot test) and stereopsis (Randot test). In some cases, we measure the subject's balance point using a dot stimulus program running on a pair of video goggles, previously validated against laboratory measurements [24], which provides us with a reference measure completely independent from the device.

A. Experimental Procedure

The experiment was conducted by a team of vision experts in Departments of Ophthalmology and Optometry. While many trial settings can be decided the on-site clinicians, we suggested the following procedure. After selecting a game strategy from the options described earlier, for each day, the participant plays between one and two hours, with a sample timeline in Table I.

Vision assessments are carried out regularly during the testing period and the operator uses the results to readjust the game contrast. The operation and measurement schedule is outlined in Table II. Visual acuity was measured with a logMAR chart with Sloan letters and stereo acuity was measured with the Randot stereo test.

B. Results

Three pilot field tests were carried out concurrently by teams of ophthalmology and optometry researchers at McGill University and the University of Waterloo, both in Canada and the University of Auckland in New Zealand. A total of nine adults, ranging from 18 to 51 years of age (average of 35.5 years), with anisometropic and or strabismic amblyopia were trained. Anisometropic amblyopia is caused by a chronic blurring of the image in one eye during early development due to an unequal refractive error between the eyes. Strabismic amblyopia is caused by a misaligned eye early in childhood. the optimal refractive correction for their amblyopic eye and if a strabismus was present, their eyes were aligned with prisms. When they were not training, the patients wore their habitual refractive correction, which often did not consist of an optimal refraction for their amblyopic eye, since this eye is traditionally thought to be unusable under normal viewing conditions. Details of the patients' best corrected amblyopic eye acuity, fellow eye/amblyopic eye contrast ratios for Tetris and stereo sensitivity are provided in Table III.

The severity of pre-training acuity loss in the amblyopic eye varied within our sample from mild (20/40) to moderate (20/125). In addition, only one third of our participants had any measurable stereoscopic depth perception prior to training and all but one participant required significantly more contrast presented to their amblyopic eye to play Tetris. The one exception (MG), only had a mild acuity loss in the amblyopic eye but had no stereoscopic depth perception, which is why training was attempted.

Despite the fact that training was relatively intermittent throughout the week, significant improvements were observed. As anticipated by the design of our paradigm, the difference in contrast between the two eyes required for Tetris play decreased significantly as a function of training ($Z = 2.52,\ p = 0.012$) with six participants able to tolerate the same contrast in both eyes after training compared to just one participant (MG) pre training. This means that the initial suppression that resulted in the information from one eye being totally ignored when viewing with two eyes was now eliminated. As a result, information from both eyes was being used for images at the same contrast, i.e., under natural viewing conditions.

Crucially, this effect in game play translated to improvements in clinical measures of visual function. There was a significant improvement in amblyopic eye acuity after training ($Z = 2.37,\ p = 0.018$) as measured by the letter acuity test, with three participants achieving sufficient acuity to no longer be considered as amblyopic according to our inclusion criteria (best corrected visual acuity of 20/40 or worse). Furthermore, there was a significant improvement in stereoscopic depth perception due to training ($Z = 2.02,\ p = 0.043$), driven by five of the nine participants. Particularly striking are participants

TABLE III

DETAILS OF AMBLYOPIC EYE ACUITY (EXPRESSED AS A DECIMAL), CONTRAST RATIO (NONAMBLYOPIC EYE CONTRAST/AMBLYOPIC EYE CONTRAST) AND STEREO SENSITIVITY (RECIPROCAL OF STEREO ACUITY IN SECONDS OF ARC) FOR EACH OF THE NINE PARTICIPANTS TESTED. VALUES ARE GIVEN FOR PRE AND POSTTRAINING. A STEREO SENSITIVITY VALUE OF 0 INDICATES NO MEASURABLE STEREOSCOPIC DEPTH PERCEPTION. NORMAL STEREO SENSITIVITY IS IN THE RANGE OF 0.05, I.E., 20 S OF ARC

Participant ID	Amblyopic Eye Acuity Pre Training	Amblyopic Eye Acuity Post Training	Contrast Ratio Pre Training	Contrast Ratio Post Training	Stereo Sensitivity Pre Training	Stereo Sensitivity Post Training	Hours of Training (mean hours per week)	Number of sessions
LB	0.40	0.40	0.71	0.83	0	0	6.25 (0.88)	13
AS	0.50	0.79	0.71	0.93	0.0017	0.0143	10.5 (1.29)	15
OH	0.50	0.79	0.43	1.00	0	0.01	7 (0.88)	19
VT	0.32	0.50	0.43	1.00	0	0.0017	12.75 (1.36)	19
AnS	0.20	0.80	0.50	1.00	0	0.0025	24.5 (7.80)	16
MW	0.16	0.20	0.33	0.64	0.0013	0.0013	13.75 (5.35)	14
MG	0.50	0.50	1.00	1.00	0	0	16 (10.18)	10
CH	0.40	0.50	0.63	1.00	0.0013	0.01	15.75 (8.48)	10
JL	0.25	0.32	0.57	1.00	0	0	35.25 (27.42)	12

OH, VT and AnS who went from no measurable stereoscopic depth perception to moderate levels of stereopsis. This suggests that the neural architecture required for stereopsis was present in these participants even though it had never previously been measurable, until suppression was reduced by training with our system [25]. The stereo results found for the majority of our participants are particularly encouraging as the current game design neither requires nor trains for stereoscopic function. We envision that at a later stage of rehabilitation, a 3-D, Tetris-style game using a similar content-splitting strategy may provide more effective treatment for stereo deficiency. Two examples of the improvement in interocular contrast as a function of training are shown in Fig. 9(a). The two participants shown here had the largest number of training sessions and therefore best demonstrate the cumulative effect of training on reduction of suppression. This pattern of results was typical of the group as a whole. Fig. 9(b) and (c) shows group performance improvements for contrast and letter acuity, respectively.

These results are consistent with two previous studies in which adults with amblyopia were repeatedly and regularly exposed to contrast balanced random dot stimuli over the course of several weeks [15], [26]. However, those previous studies exposed participants to the stimuli for an average of four weeks with at least an hour of training each weekday. Despite the less intensive exposure to the training stimulus during our pilot study, the improvements in amblyopic eye acuity we report here are comparable: an average decimal acuity improvement of 0.17 in our study versus 0.18 in the random dot studies. In addition, in both studies a number of adult amblyopic participants progressed from no measurable stereoscopic depth to clinically significant stereoscopic depth perception (3/6 in our study versus 6/7 in the random dot studies of Hess *et al.* [15]).

We are confident that the improvements we report are due to the Tetris training itself rather than to the brief one-off measurements we made using the motion coherence stimulus to assess the degree of suppression. A large number of motion coherence threshold measurements are required to achieve comparable improvements in visual function. In a previous publication ([15, Fig. 4(c)]) we outline this relationship and show that visual improvements are related to the number of blocks (each 100 individual threshold measurements) per week rather than the absolute number of blocks. Extrapolating this to the current situation we would expect no training effect from our suppression assessment measurement even for our most intensively trained subject (JL), who received an equivalent training intensity of 0.07

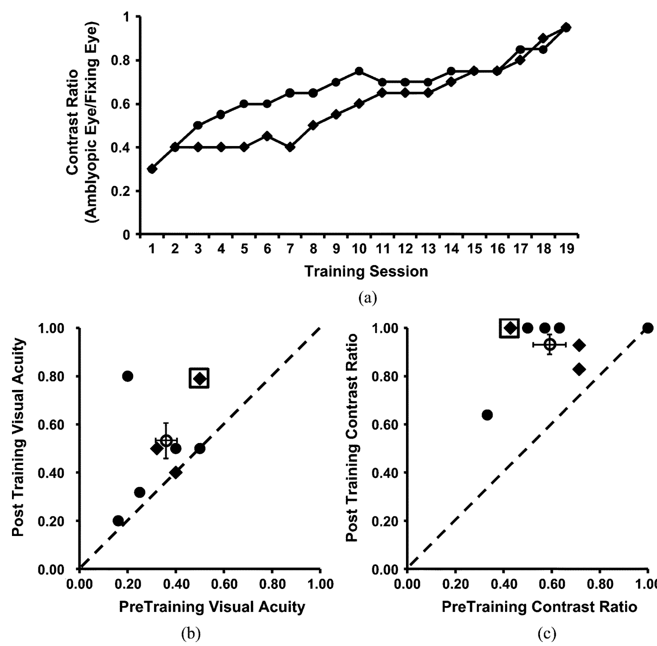


Fig. 9. Results of the training procedure for amblyopic participants. Panel A shows the improvement in the required contrast ratio between the two eyes (amblyopic eye contrast/fellow eye contrast) as a function of training session for two example participants; OH (circles) and VT (diamonds). A contrast ratio of unity indicates that no contrast imbalance between the eyes was required. Panel B shows group data for the required contrast ratio between the two eyes before and after training. Data points above the dashed unity line indicate improved binocular combination. The hollow circle indicates the group mean and error bars indicate ±1 SEM. Circular markers indicate that participants were trained using game strategy 1 and diamond markers indicate game strategy 2. A square outline signifies two overlapping data points. Panel C shows group data for amblyopic eye visual acuity before and after training. Marker designations are the same as in panel B.

blocks/week. In addition, we have shown previously that a small number of motion coherence threshold measurements can provide a stable assessment of suppression [27], indicating that limited exposure to this stimulus alone does not reduce suppression.

VI. Conclusion

We presented in this paper a working prototype of a portable gaming device designed specifically for treatment of amblyopia. The device delivers the therapeutic effect by leveraging on the contrast imbalance to encourage the interocular cooperation between the eyes, hence making the amblyopic eye contribute actively to perception. The interactive content of the game format offers the potential to engage the patients over the treatment period, while also helping the eye-care practitioner monitor the progress based on contrast level from the game. We received encouraging results from the early field tests and expect that additional improvement to the current design will further enhance the usability and therapeutic effect of this device.

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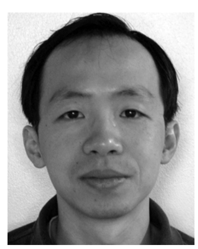

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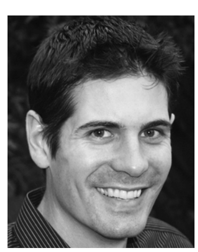

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