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The Effect of Video Game Training on the Vision of Adults with Bilateral Deprivation Amblyopia

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Abstract

Amblyopia is a condition involving reduced acuity caused by abnormal visual input during a critical period beginning shortly after birth. Amblyopia is typically considered to be irreversible during adulthood. Here we provide the first demonstration that video game training can improve at least some aspects of the vision of adults with bilateral deprivation amblyopia caused by a history of bilateral congenital cataracts. Specifically, after 40 h of training over one month with an action video game, most patients showed improvement in one or both eyes on a wide variety of tasks including acuity, spatial contrast sensitivity, and sensitivity to global motion. As well, there was evidence of improvement in at least some patients for temporal contrast sensitivity, single letter acuity, crowding, and feature spacing in faces, but not for useful field of view. The results indicate that, long after the end of the critical period for damage, there is enough residual plasticity in the adult visual system to effect improvements, even in cases of deep amblyopia caused by early bilateral deprivation.

Keywords

Deprivation amblyopia, congenital cataract, critical period, video game training, adult plasticity

1. Introduction

Amblyopia is a visual disorder involving reduced acuity that cannot be explained by an abnormality in the eye and cannot be corrected optically. It occurs when one or both eyes did not receive normal visual input during a critical period beginning

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shortly after birth. Amblyopia affects about 3% of the adult population (Attebo *et al.*, 1998; Brown *et al.*, 2000; Webber and Wood, 2005). The most common form of amblyopia, anisometropic amblyopia, occurs when unequal refractive errors in the two eyes prevented the simultaneous focusing of input on the two retinae. Also common is strabismic amblyopia, which results when the eyes were misaligned so that the brain did not receive coordinated binocular input. Least common is deprivation amblyopia, which results when patterned visual input to one or both eyes was limited by ptosis (a droopy eyelid that covers the visual axis) or a dense cataract.

When a child has an amblyopia-inducing condition, the usual treatment is to first correct the peripheral problems (to straighten the deviating eye, to correct the anisometropia with appropriate optical correction for each eye, or to surgically remove the cataractous lens and replace it with a contact lens of appropriate power). Then, in the case of monocular problems, patching the better eye is prescribed in an attempt to force usage of the affected eye. When both eyes are affected, as is the case after bilateral congenital cataracts, occlusion therapy is not recommended routinely, and treatment after surgery often consists only of monitoring the optical correction of the contact lenses designed to restore nearly normal visual input.

Although the initial problem was peripheral and can be repaired (with surgery and/or suitable optical correction), amblyopia arises at the cortical level: the abnormal early input leads to deficits in the tuning of cortical circuits. Animal studies indicate that the first level of the visual pathway with physiological abnormalities is the primary visual cortex (Le Vay *et al.*, 1980; Mitchell and MacKinnon, 2002; Mower *et al.*, 1982). In humans, the central origin of amblyopia is supported by the fact that the amblyopic eye appears entirely normal on physical examination, that the amblyopia cannot be corrected by glasses, and that there are subtle visual deficits in the fellow eye of unilateral amblyopes (Leguire *et al.*, 1990; Levi and Klein, 1985; Lewis *et al.*, 1992).

Patching treatment for amblyopia is typically tapered off around 6–7 years of age, the age at which children with normal eyes achieve adult-like acuity. In most clinical settings, no further treatment is recommended after that age based on an assumption that there will be no beneficial effect of treatment because the critical period has ended by this age (American Optometric Association, 1994). However, scattered early reports and many recent studies suggest that there is considerable residual plasticity after age 7 and that vision can be improved well beyond the end of the so-called critical period, even in adulthood. For example, in children with strabismic and/or anisometropic amblyopia, acuity improves as much when the fellow eye is patched at 11–15 years of age as when patching occurred before age 7 (Birnbaum *et al.*, 1977). Moreover, the acuity of adults with strabismic and anisometropic amblyopia has been improved by combining patching of the fellow eye with fixation exercises (Wick *et al.*, 1992) or extensive training with feedback to make subtle discriminations, such as detecting a low contrast grating or letter (Huang *et al.*, 2008, 2009), discriminating small differences in the alignment of elements (Levi and Polat, 1996; Li *et al.*, 2008), or detecting a small difference in spatial frequency (Astle *et al.*, 2010). Improvements have also been induced by repetitive transcranial magnetic stimulation over the primary visual cortex (Thompson *et al.*, 2012) and Levodopa drug therapies (Gottlob and Stangler-Zuschrott, 1990; Leguire *et al.*, 1998; Rogers *et al.*, 2003).

In adults with normal eyes, playing action video games improves acuity and contrast sensitivity, as well as enlarging the useful field of view, improving the number of moving objects that can be tracked simultaneously, and enhancing selective attention (Green and Bavelier, 2003, 2006a, b; Li *et al.*, 2009). Improvements can be induced in the laboratory after as little as 20–40 h of play of a first person shooter video game.

One recent study found that video games can also improve vision in adults with amblyopia (Li *et al.*, 2011). Specifically, acuity improved in 18 adults with strabismic and/or anisometropic amblyopia after they played a first person shooter video game (Medal of Honor) or a non-action video game (SimCity Societies) for 40 h while the fellow eye was patched. The average improvement in visual acuity was about 30%, and several amblyopes with initially mild impairments achieved normal 20/20 acuity. There were also improvements in positional acuity (detecting misalignments in sets of Gabor patches) and in keeping track of the number of objects presented together briefly, although not in every case and by different amounts across amblyopes who received the same training. Added external noise indicated that some improvement in positional acuity resulted from increased sampling efficiency (better use of the input) and some from reduced internal noise (better calibration of retinotopic maps).

The purpose of the present study was to evaluate the effect of playing an action video game for 40 h on the vision of adult amblyopic patients with a history of early bilateral deprivation. Because both eyes were amblyopic, we evaluated the impact of binocular video game playing on the vision of each eye alone and on binocular viewing. We included a large battery of tasks in the pre- and post-tests on which adults with bilateral deprivation amblyopia show deficits. To assess the effect of performing the tests repeatedly without intervening training, we included a group of control subjects with normal vision who completed the pre- and post-tests on which the patients improved but with no intervening video game training.

2. Method

2.1. Participants

2.1.1. Patients

The final sample consisted of seven adults treated for bilateral congenital cataract (mean age = 24.9 yrs; range = 19.3–30.7 yrs; 5 males). The duration of deprivation (defined as the period extending from birth until the age of first optical correction after surgery to remove the cataract) ranged from 91 to 294 days (mean = 161 days). Patients were included in the final sample only if they had been diagnosed on the first eye examination before 6 months of age with bilateral dense central cataracts that blocked all patterned visual input. Specifically, patients met the following criteria pre-treatment: (1) cataract described as dense and central and at least 4 mm in diameter, (2) the eye did not fixate or follow light, (3) no red reflex was visible, and/or (4) the cataract completely blocked the view of the fundus through an undilated pupil. All included patients had no other abnormalities in the ocular media or the retina and no other ocular disease. Patients with commonly associated abnormalities such as strabismus, nystagmus, microcornea, or controlled glaucoma with no optic nerve damage were included. A more detailed description of the inclusion and exclusion criteria has been published elsewhere (Ellemberg *et al.*, 2002; Lewis *et al.*, 1995).

Clinical details of the final sample are summarized in Table 1. Because treatment for cataract involves removing the natural lens of the eye, the patients could not focus the eye for different distances. Thus, in addition to the contact lenses (Patients 1–4 and 6) or interocular lens implants (Patients 5 and 7) which focused the eye for images at far, patients wore bifocal glasses (Patients 2, 3, 5, 6 and 7) or varifocal glasses (Patients 1 and 4) to focus the eye for images at near. In addition, the glasses corrected any residual spherical and/or astigmatic refractive errors (see last column of Table 1 for details). For each test patients wore an optical correction that maximized the clarity of the stimuli at the testing distance.

2.1.2. Visually Normal Controls

Six adults with normal or corrected-to-normal vision were recruited (mean age = 23.1 yrs; range = 19.5–30.5 yrs; 3 males). All were right-handed with handedness scores (Mondloch *et al.*, 2002) ranging from 44–50, on which a score of 30 or more is considered right-handed. In addition, all passed a visual screening exam by obtaining a score of at least $20/20^{-2}$ on the Lighthouse Distance Visual Acuity Test Chart, worse acuity with a +3 dioptre lens (to rule out farsightedness of 3D or more), fusion on the Worth 4-dot test, and perfect performance on the Randot® Test of stereoacuity. One additional participant was excluded from the visually normal sample for not meeting the screening criteria.

2.2. Overall Design

Patients played an action video game (Medal of Honor) for 40 h over the course of four weeks and completed a battery of pre-tests and an identical battery of post-tests. In addition, patients completed tests of visual acuity after every 10 h of video game play. The first 10 h of video game playing were completed in the laboratory over 2 days after the pre-test. The subsequent 30 h (recommended daily dosage: 1.5–2 h) were completed in the laboratory (Patient 5) or at home with remote monitoring by video (all other patients). Patients also completed an eye alignment exam by a certified orthoptist, the handedness questionnaire (see Table 1), and a questionnaire designed to assess their prior experience with video games.

The visually normal control group completed a subset of the pre-tests and an identical sub-set of post-tests (see Pre- and Post-test section below for details). During the intervening four weeks, the control group was instructed not to play

Table 1.
Clinical details of the seven bilateral amblyopic patients who participated in 40 h of video game training

Patient	Surgery/first optical correction (days)	Nystagmus	†Handedness	Age @ pre-test (years)	Acuity @ pre-test	Additional details
1	OD: 55/91 OS: 47/91	Latent OU: OD < OS	45 (R)	25.5	OD: 20/32 OS: 20/63	Strabismus surgery OU @ 1.5 yrs Alignment: 30^{Δ} LET 25–50% OD occlusion (1.2–7.0 yrs) Wearing CL: OD: +7.5D; OS: +5.5D and glasses to correct residual refractive error for far with varifocal add for near
2	OD: 133/181 OS: 223/294	Manifest + latent OU	49 (R)	29.4	OD: 20/100 OS: 20/40	Strabismus surgeries @ 3.2 (OS), 5.8 (OU) & 10 yrs (OD) Alignment: 2^{Δ} variable RXT → RET; 8^{Δ} LHT No occlusion Wearing CL: OD: +14.50D; OS: +16.50D and glasses to correct residual refractive error for far with bifocal add for near
3	OD: 71/91 OS: 74/91	Fine manifest + gross latent OU	50 (R)	19.3	OD: 20/63 OS: 20/63	Membrane surgery OD @ 0.8 yrs Alignment: 25^{Δ} R/AXT, 10^{Δ} RHT 15–50% OS occlusion (1.1–4.1 yrs) Wearing CL: OD: +20.00D; OS: +18.50D and glasses to correct residual refractive error for far with bifocal add for near
4	OD: 44/129 OS: 93/129	Manifest + latent OU	50 (R)	30.7	OD: 20/50 OS: 20/63	Capsular membrane needling @ 0.3 yrs 2ndary membrane & Elsching's pearl removal @ 0.8 yrs Alignment: 25^{Δ} LXT, 8^{Δ} RHT No occlusion Wearing CL: OD: +9.00D; OS: +7.50D for far and glasses to correct residual refractive error for far with varifocal add for near

Table 1.
(Continued)

Patient	Surgery/first optical correction (days)	Nystagmus	†Hand-edness	Age @ pre-test (years)	Acuity @ pre-test	Additional details
5	OD: 149/187 OS: 143/187	Fine manifest + latent OU	35 (R)	29.8	OD: 20/32 OS: 20/80	Strabismus surgery OS @ 1.7 yrs Alignment: 8^{Δ} LET, 14^{Δ} RHT 25–70% OD occlusion (4.1–6.0 yrs) IOLs @ 26.3 yrs OU; OD: +16.00D; OS: +15.00D; and glasses to correct residual refractive error for far with bifocal add for near
6	OD: 197/238 OS: 202/238	Fine latent OU	50 (R)	20.1	OD: 20/20 OS: 20/80	Strabismus surgery OU @ 10 mo Alignment: $8^{\Delta}/10^{\Delta}$ LET, slight hypotropia OS ∼35% occlusion OD (7–9 mo) Wearing CL: OD: +14.50D; OS: +15.50D and glasses to correct residual refractive error for far with bifocal add for near
7*	OD: 79/100 OS: 80/100	Manifest + horizontal latent OU	48 (R)	19.3	OD: 20/63 OS: 20/80	Strabismus surgeries @ 1.3 (OS), 1.8 (OD) & 4.8 (OU) yrs Alignment: minimal AET/AXT 15% OD occlusion (3.9–6 yrs) IOLs @ 18.8 yrs OD (+15.00D) & 18.4 yrs OS (+16.50D) and glasses to correct residual refractive error for far with bifocal add for near

† Score out of 50 on the handedness questionnaire with scores > 30 denoting right handedness (R).
OD: right eye, OS: left eye, OU: both eyes
D: dioptre, $^{\Delta}$: prism dioptre
CL: contact lens, IOL: interocular lens
RHT: right hypertropia, LHT: left hypertropia
RET: right esotropia, LET: left esotropia, RXT: right exotropia, LXT: left exotropia
AET: alternating esotropia, AXT: alternating exotropia
* The patient was trained monocularly (see Method).

any video games. The subset of tasks was chosen based on initial inspection of the data to identify tasks on which the patients appeared to improve.

2.3. Apparatus

For video game training, we used Medal of Honor: Airborne (Electronic Arts, Inc.), a first-person perspective shooting game. For training in the laboratory, we used a Sony Playstation 3™ console with the game displayed on a 27″ RCA CRT TV monitor. For video game training at home, patients used the same console connected to their personal TV monitors, and their progress was monitored *via* Skype™ and their personal webcams.

For the global motion and face perception tasks, the stimuli were created using VPixx 1.82 and SuperLab, respectively, running on an Apple Macintosh G3 computer with OS 9 and displayed on a 21″ Dell p1130 Trinitron monitor. All the other psychophysical tasks were created using MATLAB (Mathworks, 2008) with Psychtoolbox extensions (Brainard, 1997) running on an Apple Mac Pro G5 with OSX and presented on a 20″ Sony Trinitron VGA colour monitor. For the tasks requiring fine contrast manipulations (spatial and temporal contrast sensitivity and estimating the contrast threshold in external noise), we used a special circuit (Li *et al.*, 2003) to produce monochromatic signals at fine grayscale resolution (>12.5 bits) combined with a lookup table, generated by psychophysical matching judgments, that linearly translated pixel gray-levels into display luminance.

2.4. Procedure

The experimental protocol was approved by the Research Ethics Boards of McMaster University and The Hospital for Sick Children, Toronto. Upon arrival of the subjects, the procedure was explained to the participants and consent was obtained. Patients received $10/h for their participation in the pre- and post-tests and video game playing in the laboratory. Upon completion of the study, they were also given the video game console and game used during training. Normal controls received $10/h for their participation in the subset of the pre- and post-tests.

To evaluate video game experience prior to the study, we first had the patients complete a video game questionnaire that asked about duration and frequency of video game playing for various categories of games (action, fighting, strategy, fantasy, and sports games). Six of the seven patients (Patients 1–6) were categorized as novices. We began training for these patients at the entry level of difficulty and had them play the game while viewing binocularly with the contrast of the TV set at approximately 75% of its maximum. Patient 7 (denoted as 7* in the figures) was classified as an expert game player because he had played first-person shooter games (e.g., Halo 3 or Call of Duty) on average 2.5 h per week during the previous 6 months. To make game playing more challenging for him, we began his training at the intermediate difficulty level with the contrast of the TV lowered to approximately 30% of its maximum and had him play while viewing monocularly with his worse eye (defined on the basis of acuity at the pre-test).

All controls were classified as novices because they indicated that they had played first-person shooter games less than one hour per week during the previous 6 months.

2.5. Video Game Training for Patients

During the first 10 h of training, the experimenter watched the patients play the game in the laboratory and provided tips and advice when necessary. Patients were given a break after every 2 h of play. Then, six of the seven patients were sent home with the console and game for the next 30 h of training. Their play was logged remotely and monitored by the experimenter *via* online videoconference. Video conferences were set up at the patients' convenience with the restrictions that all 30 h of home play would be monitored, that patients would play 10 h per week, that play would be completed within 3 weeks, and that no other video game playing would occur during this interval. With the patients' approval, some of the game playing was recorded. One patient (Patient 5), who lived nearby, commuted to the laboratory for all 40 h of training.

2.6. Pre- and Post-Tests

Before video game training, patients completed three clinical tests of vision (monocular and binocular linear letter acuity, fusion, and stereopsis), two questionnaires (NEI-RQL42 and Ryff's 54-item scale of Psychological Well-being), and seven psychophysical tests (crowding, spatial and temporal contrast sensitivity, contrast thresholds in external noise, sensitivity to global motion, face perception, and useful field of view). As in similar previous studies (e.g., Mondloch *et al.*, 2002), patients completed the face perception task binocularly. The remaining six psychophysical tasks were each completed three times: once binocularly and once with each eye tested monocularly. Prior to each psychophysical test, patients were provided with a full practice run (1) to ensure that they understood the task and (2) to stabilize their performance.

Patients 1–5 and Patient 7 repeated the entire pre-test protocol during the post-tests following video game training, a process that took 7–8 h. Because of unexpected personal circumstances, Patient 6 was able to complete only a subset of the post-tests.

The normal control group completed a subset of the full battery of tasks during pre-test and 4 weeks later during post-test, namely, the three clinical tests of vision (monocular and binocular linear letter acuity, fusion, and stereopsis) and the psychophysical tests on which the patients seemed to improve after video game training. Specifically, of the seven psychophysical tests described below, the normal control group completed spatial and temporal contrast sensitivity under monocular and binocular viewing conditions, contrast thresholds in external noise under monocular viewing conditions only, sensitivity to global motion both under monocular and binocular viewing conditions but only at 4 $\mathrm{deg{\cdot}s^{-1}}$, and the complete set of face perception tasks.

Like patients, normal controls completed a full practice run prior to each psychophysical test. The entire subset of pre- and post-tests each took approximately 4 h for the control group to complete.

2.6.1. Clinical Tests

We measured linear letter acuity monocularly in each eye and binocularly using two versions of the Lighthouse Eye Chart (2nd edn, Category number C105 and 2175) to reduce practice effects. We measured fusion with the Worth 4-dot test and stereopsis with the Randot® test. To gauge patients' self evaluation of the impact of their visual deficits and any improvement on their everyday lives, we administered the NEI-RQL42 Refractive Error Quality of Life Questionnaire (Hays *et al.*, 2003) and Ryff's 54-item scale of Psychological Well-being (Ryff, 1989).

2.6.2. Psychophysical Tests

(1) Crowding. A sample stimulus used to test crowding is illustrated in Fig. 1A. The method to measure crowding was identical to that used by Jeon *et al.* (2010) for Patient 1 but included minor modifications for subsequent patients. Briefly, for Patient 1, we used a 2-alternative forced-choice procedure to first measure single letter acuity and crowding. In each trial, the patient was shown a single black Sloan letter E (characterized by an equal height and width, with the height equal to 5 times the stroke width), randomly rotated either 90° ('up') or 270° ('down') from its upright position. The task on each trial was to identify verbally the whereabouts of the stems of the rotated E.

For the single letter task, the target letter E was presented for 500 ms, with an initial stroke width of 5 arcmin when viewed from 424 cm. The experimenter entered the patients' verbal responses into a computer. After each response, visual and auditory feedback were provided to indicate whether the response was correct. We used a 3-down-1-up staircase to determine the smallest stroke width at which the patient could reliably discriminate the target orientation 79.1% of the time. The initial step size was one octave (where an octave is a halving or a doubling of a value) and decreased to one half octave after the first three reversals, and decreased further to one-quarter octave from the sixth reversal. The staircase was terminated after 10 reversals, and the threshold stroke width of the letter E was calculated from the geometric mean of the last six reversals.

After completing the single letter acuity test, the patient was then tested with the target E surrounded by flanking bars. To ensure that the negative effect of flankers on target discrimination was caused mainly by crowding and not the difficulty of seeing the single letter at threshold, the target E was presented at either a minimum of a one pixel increase from the single letter threshold or 1.2 times that threshold, whichever was bigger. The crowding stimuli consisted of an E flanked by four sets of three black bars. Each flanking bar had the same stroke width as the stems of the E. The spatial extent of the set of three flanking bars was the same as that of the E, and their orientations were randomized for each trial. The task on each trial was to verbally report whether the orientation of the letter E in the centre of

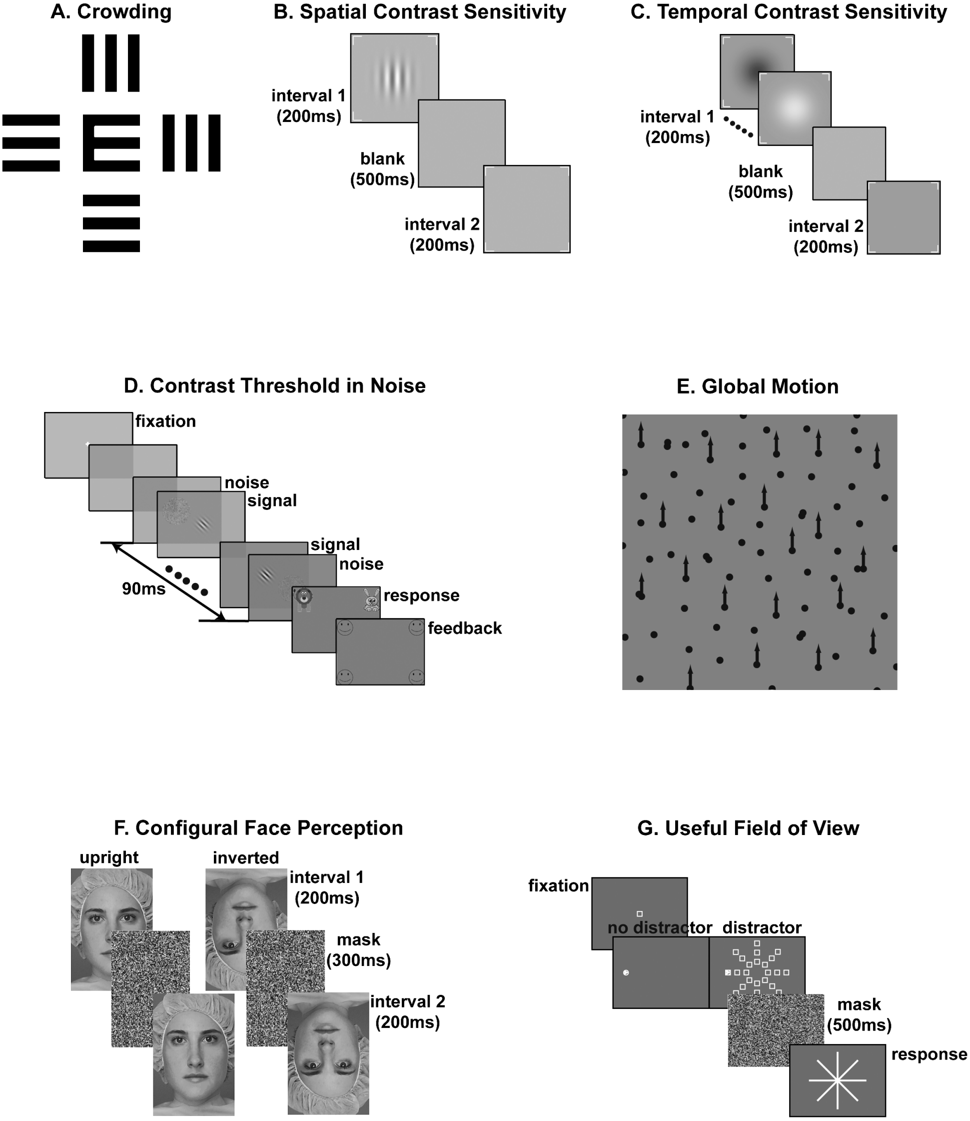

Figure 1. Examples of tasks included in the pre- and post-test battery. *Task A*. An example of a stimulus used in the crowding task. Patients discriminated the orientation of the letter E surrounded by 3-bar flankers of the same size as the letter. The orientations of the flankers were determined randomly trial by trial. Crowding threshold was defined as the distance required to discriminate the orientation of the central letter 79.1% of the time. The size of the E was determined by the patient's single letter acuity. *Task B*. A sample trial sequence used to measure the spatial contrast sensitivity function. Patients indicated which of the two intervals contained a sine-wave grating that varied in contrast and spatial frequency. In both intervals, white, caret-shaped stimulus placeholders appeared to demarcate where the grating might appear.

the entire configuration was up or down. The separation of the flanking bars from the target varied over trials according to the same 3-up-1-down staircase procedure used to measure single letter acuity. We calculated the geometric mean of the last six reversals and defined crowding threshold as the minimum separation between the nearest edges of the flankers, in multiples of stroke width of the central letter, for which the orientation of the target E was judged accurately 79.1% of the time.

The procedure for subsequent patients was identical except we used a 4-alternative rather than a 2-alternative forced-choice procedure, and patients viewed the stimuli from 212 cm. Specifically, the letter ‘E’ was now rotated in one of four directions (either by 0°, 90°, 180° or 270°), and the task on each trial was to indicate whether the stems were pointing right, left, up, or down. We also increased the number of reversals in the test from 10 to 12. These modifications were intended to increase the sensitivity of the test.

(2) Spatial Contrast Sensitivity. We used a 2-interval forced-choice procedure in which the participants identified which one of two intervals contained a patch of sinusoidal grating ($14^\circ \times 14^\circ$ at a viewing distance of 114 cm) that was vignetted by a Gaussian envelope (see Fig. 1B). The luminance profile of the grating is described by the following equation:

$$L(x, y) = c\cos(2\pi f x)\mathrm{e}^{\{-(x^2+y^2)/2\sigma^2\}},$$

where c is contrast, σ is the standard deviation of the Gaussian envelope (3°), and f is spatial frequency of the sinusoidal grating. The other interval contained a gray background with a luminance equivalent to the mean of the grating. Each trial began with a key press. The first and the second intervals of a trial each came on for 200 ms

Figure 1. (Continued.) *Task C.* A sample trial sequence used to measure the temporal contrast sensitivity function. Patients indicated which of the two intervals contained a flickering pattern that varied in contrast across four temporal frequencies. As in measuring spatial contrast sensitivity, caret-shaped placeholders were presented in each interval to demarcate the area where the grating might appear. *Task D.* A sample trial sequence used to measure contrast thresholds in noise. After a fixation cross, patients discriminated the orientation of a sine-wave grating that was temporally interleaved with noise frames. Contrast thresholds were measured in noise, the strength of which varied across trials. *Task E.* A static illustration of the global motion display. The dots with arrows represent signal dots moving upward. The remaining dots represent noise dots moving in random directions. Thresholds were defined as the minimum percentage of coherently moving signal dots necessary for accurate identification of upward or downward motion. *Task F.* A sample trial sequence for the facial processing task. For both upright and inverted sequences, each member of a pair of faces was flashed briefly and separated by a noise mask. Patients judged if the members of the pair were the same or different. *Task G.* A sample trial sequence for the Useful Field of View (UFOV) task. After a fixation box appeared in the middle of the screen, the target (small white triangle) enclosed in a square flashed briefly in one of 24 locations distributed across three eccentricities. After a noise mask, patients indicated on the radial spoke where the target had appeared. In the no-distractor condition, only the target enclosed in a square appeared before the mask. In the distractor condition, both the target and the square placeholders of all possible target locations appeared simultaneously.

and were separated by a blank 500 ms interval. Both stimuli were demarcated by caret-shaped white stimulus placeholders at the four corners of the area where a grating could occur so that patients could recognize the intervals even when the contrast of the grating was at or below threshold. No feedback was provided.

For the first patient tested (Patient 1), we used a 3-up-1-down staircase procedure to measure the minimum contrast necessary to accurately discriminate the grating from a blank field 79.1% of the time. The initial contrast was 25% and the initial step size was one octave. The step size decreased to a half octave after the first two reversals and the staircase terminated after 10 reversals or a maximum of 80 trials, whichever was reached first. The threshold was taken as the geometric mean of the last six reversals. The procedure was repeated for six spatial frequencies (0.33, 0.5, 1, 2, 4, and 8 cpd) presented in an increasing order.

To reduce testing time, the remaining six patients and all of the controls were tested using the quick-CSF (*qCSF*) method (Lesmes *et al.*, 2010), a Bayesian adaptive procedure applying a strategy developed to estimate specific parameters of the psychometric function (Kontsevich and Tyler, 1999). Before each trial, a one-step-ahead search found the ‘optimal’ set of stimulus parameters (spatial frequency and contrast) of the sinusoidal grating that maximized the expected information gain about four parameters of the contrast sensitivity function (peak sensitivity, peak frequency, the bandwidth of the contrast sensitivity function, and the truncation at the low spatial frequency region). With the *qCSF* procedure, the entire contrast sensitivity function was estimated in only 300 trials.

(3) Temporal Contrast Sensitivity. We used a 2-interval forced-choice procedure to measure the participants’ ability to detect the interval containing a flickering signal from the interval containing only a stationary gray background (see Fig. 1C). The flickering signal consisted of a 2-dimensional Gaussian (5.14° × 5.14° at a viewing distance of 50 cm) profile with a standard deviation of 3°, the luminance of which was sinusoidally modulated with different temporal frequencies. Temporal contrast sensitivity was tested at 30, 20, 10, and 5 Hz, in the corresponding order. Other details of the method were identical to that described for the test of spatial contrast sensitivity for Patient 1.

(4) Contrast Threshold Function across External Noise. We used the quick-*TvC* method (Lesmes *et al.*, 2006) to measure multiple contrast thresholds for stimuli embedded in differing amounts of external noise (see Fig. 1D). The quick-*TvC* (*qTvC*) method is based on Bayesian principles similar to those desribed above for *qCSF*. The signal was a Gabor oriented ±45° from vertical. The luminance profile of the stimulus is described by the following equation:

$$L(x, y) = L_0[1.0 + c\sin\{2\pi f(x\cos\theta + y\sin\theta)\}]\mathrm{e}^{\{-(x^2+y^2)/2\sigma^2\}},$$

where c is signal contrast, σ is the standard deviation of the Gaussian window (1°), f is frequency (1 cpd), and L_0 is the background luminance, which was set to the middle of the dynamic range of the display. The Gabor stimulus and noise patches were 7.8° × 7.8° when viewed from 57 cm. An external noise patch was composed of 0.1° × 0.1° pixel granules, whose contrasts were independently sampled in each trial from a Gaussian distribution with a mean of 0 and standard deviation truncated at ±3.

At the beginning of each trial, participants fixated a white cross (0.6° × 0.6°) presented in the centre of the monitor for 500 ms, followed by a 250 ms blank screen prior to the onset of the test stimulus. The test stimulus was a sequence of nine alternating 10 ms patches of noise and signal in the following order: noise_1-signal_1-noise_2-$\cdots$-noise_4-signal_4-noise_5, which totaled 90 ms. The alternation of the noise and the Gabor patches was fast enough that the noise appeared to be spatially superimposed on the Gabor. Immediately after the test stimulus, there appeared a response screen that consisted of an image of a cartoon lion in the upper left corner of the screen and an image of a cartoon rabbit in the upper right corner of the screen. Each image was 12° wide and 12° high, and a white question mark was centred between them. This screen was presented until participants responded by pressing one key when they judged the grating to be oriented to the left of vertical and another when they judged it to be oriented to the right of vertical. Visual and auditory feedback were provided after each response, consisting of four happy faces and cheering sounds (e.g., clapping) for correct responses and four sad faces and a ‘doh!’ sound for incorrect responses.

(5) Global Motion. A sample stimulus for global motion is illustrated in Fig. 1E. The perception of global motion was examined using random-dot kinematogram (RDK; Newsome and Paré, 1988) displays. Coherence thresholds were measured at the two speeds of 4 and 18 $\text{deg}\cdot\text{s}^{-1}$ in separate blocks for patients but only at the slower speed for controls. During each trial, a randomly chosen subset (signal) of 300 black dots (0.5° in diameter when viewed from 50 cm) was constrained to move in the same direction (upward or downward) at a specified speed for a number of frames. Remaining dots (noise) in the display moved at the same speed but in random directions, covering the entire 360° range. Signal strength, defined as the proportion of signal dots, was varied by the rules of a variant of ML-PEST procedure (Harvey, 1986).

To assure that the overall direction of motion could not be determined by local motion detectors, the dots were assigned random birthdates and each dot was replaced after a lifetime of 200 ms (15 frames) or 400 ms (30 frames) for the slower and faster speeds, respectively. At the end of its lifetime, the dot was redrawn in a new, random location in the display area, before resuming its motion. Thus, on every frame, some dots, chosen randomly from the entire group of dots, were reborn. The direction of the global pattern could thus be determined only by integrating the local signals over a larger summation field and not by following a single dot. Patients were instructed to fixate a red cross at the centre of the screen, which disappeared during the 2-s presentation of the RDK, and were asked to judge whether the overall direction of motion produced by the signal dots was upward or downward. No feedback was provided.

(6) Sensitivity to Configural Cues to Facial Identity. We measured sensitivity to second-order relations in faces (the spacing of internal features) (see Fig. 1F) using stimuli and procedures described previously by Mondloch *et al.* (2002) except that we tested only three conditions in the following order: spacing upright (30 trials), spacing inverted (30 trials), and a third condition with completely different faces (32 trials). Briefly, in the upright and inverted spacing conditions, the stimuli were a set of five faces (5.7° × 9.1° from the viewing distance of 100 cm). Four of the faces ('sisters') were created by modifying the spatial relationship between the eyes and mouth of a template face called 'Jane'. On each trial, one of the five possible faces appeared for 200 ms, and following a mask for 300 ms, a second face appeared until the patients indicated whether the pair was the same or different. The correct answer was the same for half the trials. No feedback was provided. The task for the third condition was identical except that the stimuli consisted of five completely different faces. The purpose of this third condition was to determine if the patients were still 'playing the game' at the end of the procedure. We calculated the accuracy in each condition.

(7) Useful Field of View (UFOV). We measured patients' ability to detect peripheral targets at three eccentricities (10°, 20°, and 30°) with and without the presence of distracting stimuli in the preiphery (see Fig. 1G). Patients were tested first with the no-distractor condition. Here, a white outline of a square appeared first as a fixation square (4° × 4° when viewed from 24 cm), and following a 500 ms interstimulus interval, a target (a white triangle within a white circle; 3° × 3° when viewed from 24 cm) appeared on one of eight meridia (on the horizontal, vertical, or one of two diagonal meridia). After a mask of 500 ms, patients indicated the meridian on which the target had appeared. We used three interleaved 3-down-1-up staircases for the three eccentricities to determine the minimum duration required to reliably detect the target 79.1% of the time. Starting with an initial 150 ms duration, the initial step size was two monitor refreshes and decreased to a single refresh after the first three reversals. The three staircases were randomly interleaved until 11 reversals were reached, and the threshold duration was calculated from the mean of the last 10 correct trials. The no-distractor condition ended once all staircases had been terminated.

For the distractor condition, the procedure was the same except that each possible target position was surrounded by the outline of a square formed from white lines, identical to the fixation square.

3. Results

Figures 2–9 show the pre- and post-test results of patients and those of normal controls for the subset of tasks that they completed. In all graphs, Patient 7 is marked by an asterisk (*) to denote the fact that he completed video game training monocularly with his worse eye, rather than binocularly as was the case with all other patients. Accordingly, for monocular tests, only results from his worse eye (the only eye receiving video game training) are included. For patients, figures are arranged to show results for the worse eye on the left, for the better eye in the middle, and for binocular tests on the right side except for face perception, which was tested only binocularly. For all but Patient 3, we defined the worse eye by acuity at the pre-test. Because Patient 3 had equal acuities in the two eyes (see Table 1), we defined the right eye as the worse eye based on alignment history. Figures for the normal control group are arranged to show monocular results on the left and binocular results on the right. Because there is no reason to expect different performance for the right and left eyes of normal controls, we used the mean (or the geometric mean where appropriate) of the results from the right and left eyes to gain a more stable estimate of monocular performance for each measure tested monocularly. All panels of Figs 2, 3, 7, 8, and 9 are plotted so that improvements from pre- to post-test are indicated by values above the dotted identity line.

(1) Linear Letter Acuity and Stereo Vision. To assess the changes in acuity before and after the 40 h of training, we have plotted the patients' acuities (measured in log minimum angle of resolution) from pre- to post-test in Fig. 2A. The black cross in each panel represents the mean acuity with a vertical stroke at the mean for the pre-test and a horizontal stroke at the mean for the post-test with the standard error in each case indicated by the length of the stroke. After 40 h of training (1.5–2 h/day), acuity improved in five of seven patients viewing with their worse eyes and in six of seven patients viewing binocularly. In the other cases, there was no change (1 worse eye, 1 binocular test) or a small decrement (1 worse eye). There was little evidence of improvement in the better eye. On average, patients improved 0.1 logMAR (equivalent to a 1 line difference on a letter chart) in their worse eyes and when tested binocularly. Initially, all the patients were stereo-blind with diplopia (double vision) and remained so throughout the study.

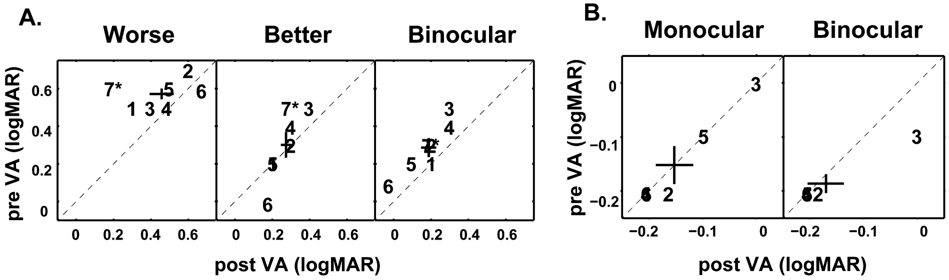

Figure 2. Panel A shows patients' visual acuity (VA) in log minimum angle of resolution (logMAR) when tested with the worse eye alone (left panel), the better eye alone (middle panel), and binocularly (right panel) before (pre) *versus* after (post) the 40 h of video game training. The black cross in each panel represents the mean acuity with a horizontal standard error of the mean for the post-test acuity and a vertical standard error of the mean for the pre-test acuity. Panel B shows logMAR changes in normal controls between pre- and post-test without training. The format is the same as in Panel A except that the mean of their results from each eye tested alone are combined under the monocular graph.

Figure 2B shows the acuity changes in normal controls from pre- to post-test without video game training. In contrast to the patient group, there is no sign of improvement in any case.

(2) Single Letter Acuity and Crowding. Figures 3A and 3B show, respectively, changes in the patients' single letter acuity and crowding before *versus* after the 40 h of training, plotted in the same way as Fig. 2 for linear letter acuity. As shown in Fig. 3A, there was little change in mean single letter acuity, although about half of the patients showed some improvement in each case. On the other hand, as shown in Fig. 3B, video game playing seemed to be effective in reducing the deleterious effects of crowding in four out of six worse eyes. However, there was no improvement in the better eyes or on binocular tests.

(3) Spatial Contrast Sensitivity. To assess changes at specific spatial frequencies after video game play, we calculated the ratio between the post-sensitivity value and the pre-sensitivity value. PPRs $>$ 1.0 represent an improvement in contrast sensitivity between the pre- and post-test whereas PPRs $<$ 1.0 represent deterioration in contrast sensitivity. PPR $=$ 1 represents no change in contrast sensitivity before *versus* after the training. Figure 4A summarizes these data by showing, for each spatial frequency, the mean of the individual PPRs for the seven patients. Note that the number of patients for some spatial frequencies and eye conditions is less than seven because Patient 1 was tested at only six spatial frequencies (see Methods), and some patients were unable to see the finer gratings even at the highest contrast. As shown in Fig. 4A, there were overall improvements in contrast sensitivity for

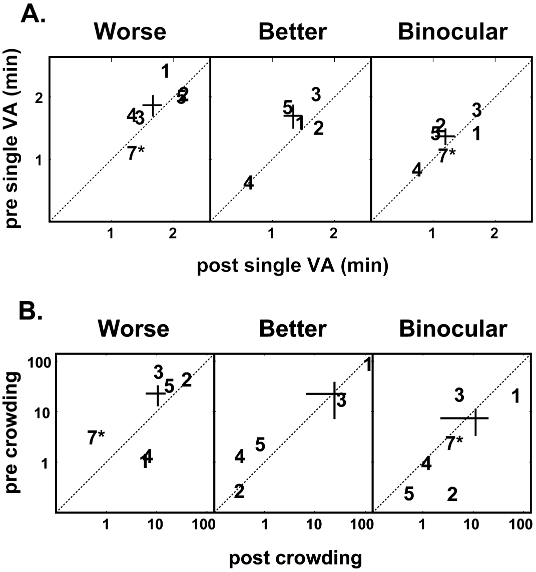

Figure 3. Single letter acuity (Panel A) and crowding (Panel B) before *versus* after 40 h of video game training. Other details as in Fig. 2A.

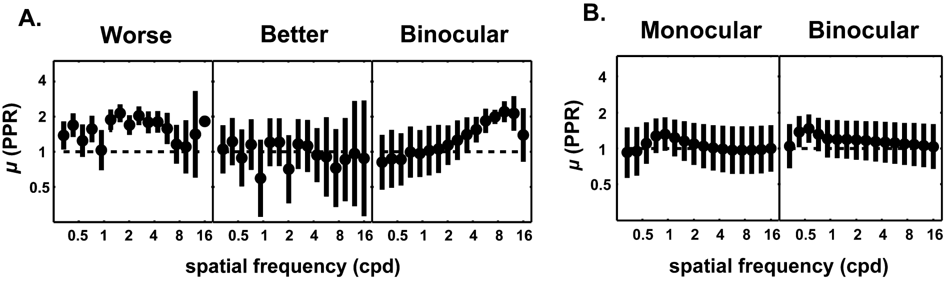

Figure 4. Panel A shows the mean change (±1 *s.e.*) in sensitivity across spatial frequencies before and after video game training when tested with the worse eye, the better eye, and binocularly. Pre- and post-ratios (PPR) were calculated by dividing post-sensitivity by pre-sensitivity; PPR = 1 represents no change, PPR > 1 represents improvement, and PPR < 1 represents deterioration. Panel B shows the mean change (±1 *s.e.*) in sensitivity across spatial frequencies without training when normal controls were tested monocularly and binocularly. Other details are same as in Fig. 4A.

mid-spatial frequencies (i.e., 2–4 cpd) in monocular tests of the worse eye and for mid- and high spatial frequencies (>4 cpd) under binocular viewing conditions. However, there was no evidence of improvements for any spatial frequency when the better eye was tested alone.

Figure 4B shows the mean pre- to post-sensitivity ratios for normal controls in monocular and binocular viewing conditions. In both viewing conditions, normal controls showed little or no change in performance.

(4) Temporal Contrast Sensitivity. Figures 5A and 5B follow a format similar to that described for spatial contrast sensitivity in showing the change in temporal contrast sensitivity between the pre- and post-test for patients and normal controls, respectively. Figure 5A shows the mean sensitivity ratios per eye condition before *versus* after the video game training. Although the mean sensitivity ratios are above 1 for the monocular tests of both the worse and better eyes, the marked variability indicates that the improvements did not occur in every patient. With the worse eye, five of the seven patients improved at 10 Hz and six of the seven at 20 Hz. With the better eye, four improved at 10 Hz and five at 30 Hz. There was no hint of improvement under binocular conditions.

Figure 5B shows the average sensitivity change of normal controls for the temporal frequencies tested between pre- and post-tests. In general, there is no evidence for a change under either viewing condition.

(5) Contrast Threshold across External Noise. Figure 6A shows the patients' average contrast thresholds with half of the error bars measured across varying amounts of external noise before (gray symbols) and after (black symbols) 40 h of video game play. Given the variance, it seems that there was no effect of training on performance in any of the viewing conditions.

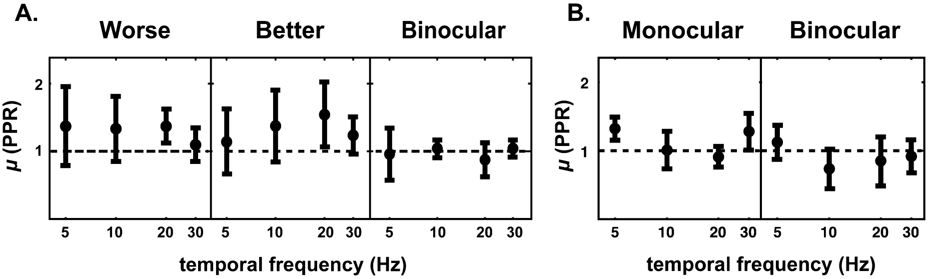

Figure 5. Temporal contrast sensitivity changes for patients (Panel A) and normal controls (Panel B). Details are same as in the corresponding panels of Fig. 4.

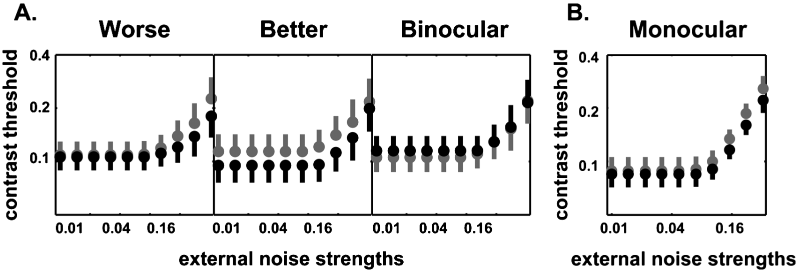

Figure 6. Panel A shows the mean contrast threshold as a function of external noise strength averaged across seven patients tested under the three viewing conditions (worse eye, better eye, and binocularly) except for the Patient 7 who was tested only with his worse eye. Each dot represents the mean threshold (+1 standard error) measured using the quick-*TvC* method before (gray symbols) and after (black symbols) video game play. Panel B shows mean contrast thresholds across external noise strength for five normal controls (one of the subjects was not able to do the task) when tested monocularly.

Figure 6B shows the results of the normal controls, all of whom viewed the stimuli only monocularly. The two curves (pre- and post-tests without training) essentially overlap, a pattern that indicates no change in performance.

(6) Global Motion. Figure 7 shows changes in the patients' motion coherence thresholds for dots moving at 4 deg·s^{-1} (Fig. 7A) and 18 deg·s^{-1} (Fig. 7B) before *versus* after the 40 h of training. The data are plotted in the same format as Fig. 2. (Patient 6 was tested only at the slower speed.) Coherence thresholds improved when patients were tested binocularly, both for dots moving at the slower speed (Fig. 7A) and at the faster speed (Fig. 7B). Although some patients improved when tested monocularly with the worse and/or better eye, the mean improvements in those conditions were at or close to zero.

Figure 7C shows changes without video game training between pre- and post-test in motion coherence thresholds for dots moving at 4 deg·s^{-1} in the normal controls. There was no apparent change in performance either when tested monocularly or binocularly.

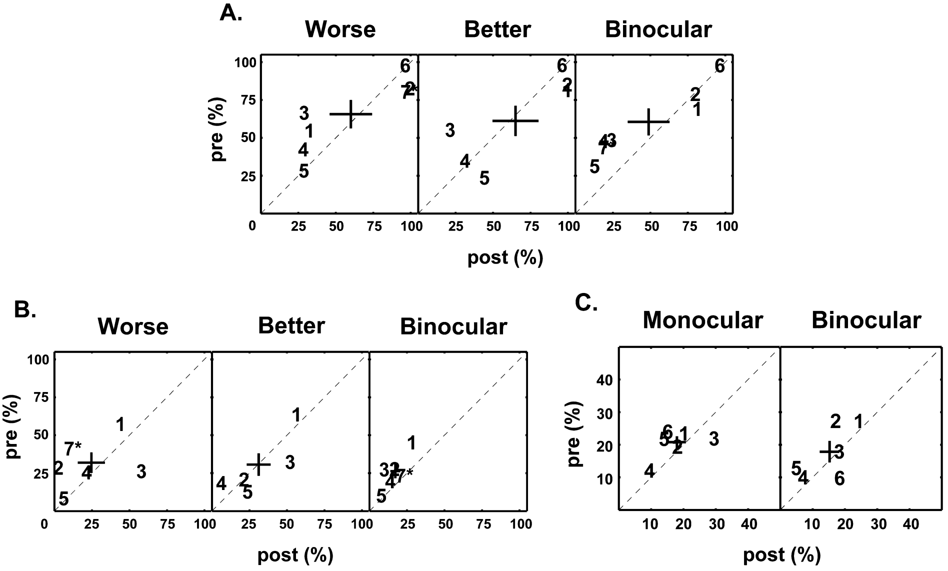

Figure 7. Global motion coherence thresholds with the speeds of 4 deg·s^{-1} (Panel A) and 18 deg·s^{-1} (Panel B) for patients. Panel C shows global motion coherence thresholds with the speed of 4 deg·s^{-1} for normal controls (the faster speed was not tested). Other details are the same as in Fig. 2.

(7) Configural Face Processing. Figure 8A shows changes before *versus* after the 40 h of video game playing in patients' ability to discriminate feature spacing for upright (left panel) and inverted (right panel) faces. As shown by the location of the error bar, video game playing improved patients' ability to discriminate upright faces only modestly (left panel) but any improvement was similar for inverted (right panel) faces. Thus, video game playing appears to have influenced general sensitivity to differences in feature spacing without influencing patients' expertise for upright faces.

Figure 8B shows the results from the normal group: simply repeating the same task twice results in no improvement in the ability to discriminate upright or inverted faces.

(8) Useful Field of View. Figure 9 shows the changes in the useful field of view for tests with no distractors (Fig. 9A) and tests with distractors (Fig. 9B) before *versus* after the 40 h of video game play. Results are for target locations at 10° (top panels), 20° (middle panels), and 30° (bottom panels). Most patients' performance was unchanged and there is no evidence of improvement in the location of the black crosses in any of the conditions.

4. Discussion

The results indicate that 40 h of playing an action video game is sufficient to induce some improvement in the visual perception of adults with bilateral deprivation

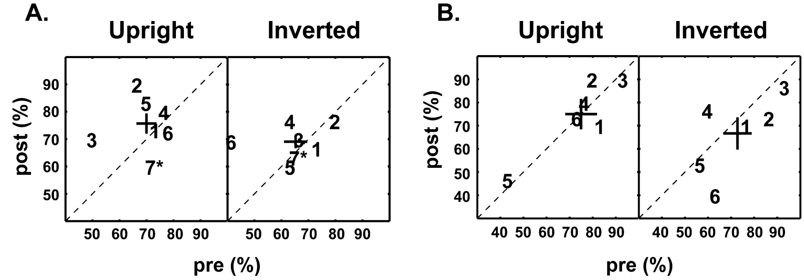

Figure 8. Panel A shows accuracy on the test of configural face perception before (pre) *versus* after (post) 40 h of video game play. Data for upright faces are shown in the left panel and for inverted faces on the right panel. All testing was completed only under binocular viewing conditions. Panel B shows the results for normal controls with the same format as Panel A. Other details are the same as in Fig. 2, except the locations of the axes for pre- and post-test were reversed so that, as in previous figures, improvements from pre- to post-test would still be indicated by values above the dotted identity line.

amblyopia. This is the first demonstration in humans that some recovery from deprivation amblyopia is possible even in adulthood, long after the end of the critical period during which the system can be damaged by abnormal input. It is consistent with recent evidence that the vision of adults with strabismic or anisometropic amblyopia can be improved by 40 h of playing the same action video game (Medal of Honor), 40 h of playing a more social video game (Sims) (Li *et al.*, 2011), or extensive perceptual training with feedback on a specific visual task such as grating detection or gabor alignment (Chung *et al.*, 2006; Levi and Polat, 1996; Polat *et al.*, 2004). It is also consistent with evidence from rodent models of (monocular) deprivation amblyopia showing that environmental enrichment can alter ocular dominance and improve visual acuity even when enrichment is introduced in adulthood (Sale *et al.*, 2007).

The video game training used here induced some improvement in most patients on a diverse set of tasks: acuity (linear letter), spatial contrast sensitivity, and sensitivity to global motion. Some patients improved, as well, on other tasks in the battery. Similarly, the previous study using video game training with adults with strabismic or anisometropic amblyopia found some improvement in a variety of visual tasks, including linear letter acuity, positional acuity (sensitivity to small misalignment of gratings), visual counting (counting the number of objects flashed briefly on the screen), and stereoacuity. The benefits of perceptual training on a specific visual task for adults with strabismic or anisometropic amblyopia are usually less general: there is usually improvement on linear letter acuity and on the trained task, with broader transfer if the training was near threshold (Huang *et al.*, 2008; Zhou *et al.*, 2006) or if it included multiple conditions (Polat *et al.*, 2004). Video game training may transfer more broadly because it demands fast responses to many types of stimulus change that are titrated to the player's current level of skill.

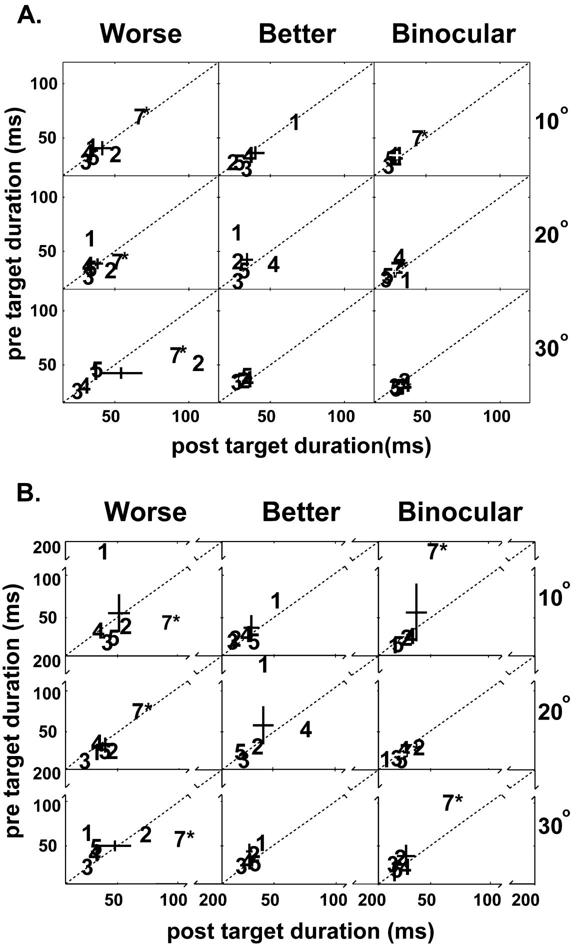

Figure 9. Duration of target presentation for Useful Field of View in tests without distractors (Panel A) and with distractors (Panel B). Other details as in Fig. 2A.

As in most previous studies of training adult amblyopes, we cannot rule out the possibility that some of the improvement resulted from performing a task for a second time during the post-test, that is, from practicing the task rather than from the intervening video game play. However, that alternative explanation seems unlikely for several reasons. First, the results from the normal control group showed that simply repeating the same task twice over the same interval as the pre- and post-tests in patients, but without the intervening video game traning, did not induce any significant changes in visual sensitivity. This outcome is in marked contrast to that of typical adults who played an action video game in the laboratory (Green and Bavelier, 2003; Li *et al.*, 2009, 2011) or the patients in this study, who showed improvements in one or both eyes on multiple measures from pre-test to post-test. Second, previous testing of this cohort has revealed no improvement in acuity despite repeated testings, and no improvement in contrast sensitivity, global motion, or sensitivity to feature spacing in faces when the tasks were repeated 1–3 years apart after age 10. Third, we used different versions of the acuity chart across the tests to minimize any benefit from learning the letters on a particular chart. Fourth, to minimize the contribution of practice on the tests, except for the clinical and face perception tasks, we included a full practice run prior to taking the pre-test and post-test measurements.

Nor is it likely that any improvements from pre-test to post-test in the patient group were nothing more than random fluctuations from unstable pre-test assessments. The pre-tests were thorough, taking a total of eight hours to complete, and followed the full practice run. For some tasks, such as *qCSF* and *qTvC*, the full practice session included the same 300 trials as in the experimental session. Including a full practice session before the tasks was designed to minimize the effect of initial variations in learning and so stabilize performance, thus yielding accurate estimates of pre-test performance.

4.1. Changes in Low-Level Vision

Most patients (five out of seven) showed improved linear letter acuity in the worse eye, an improvement that averaged one line. This improvement is somewhat smaller than that obtained in the video game training study with adults with strabismic and/or anisometropic amblyopia (1.6 lines) (Li *et al.*, 2011). However, patients appeared to be able to make use of the improved vision in the worse eye when tested binocularly: six of the seven patients improved, with an average improvement of one line. The improvement appeared to reflect an improvement in sensitivity to mid- and high spatial frequencies, combined, in some patients, with some reduction in crowding and/or improvement in single letter acuity. There was less evidence of improvement in the better eye: more modest changes in linear letter acuity and essentially no change in crowding or sensitivity to spatial frequency. The improvements observed here are consistent with evidence that the spatial contrast sensitivity of adults with normal vision can be enhanced if they play an action video game in the laboratory for 50 h over 9 weeks (Li *et al.*, 2009). Improved linear acuity, reduced crowding, and/or improved spatial contrast sensitivity have also been demonstrated in adults with normal vision given perceptual training on the identification of low-contrast letters (e.g., Chung *et al.*, 2007) and in adults with strabismic or anisometropic amblyopia given perceptual training on the detection of a low contrast grating (e.g., Huang *et al.*, 2008), dectection of a slight misalignment between two stimuli (e.g., Levi and Polat, 1996), or identification of low contrast letters (Chung *et al.*, 2006). Like those forms of perceptual training, Medal of Honor requires the detection of objects of varying size and contrast under highly motivating conditions.

Despite the improvements in binocular acuity, there was no improvement in binocular fusion or stereopsis. All seven patients saw five dots when tested with the Worth 4-dot test at both the pre- and post-test and during the intermediate testings, a result indicating that they perceive the inputs received from each eye but are unable to fuse them, perhaps because their eyes are not perfectly aligned (see Table 1). Their ability to use the non-fused input, without suppressing input from either eye, is likely critical to the observed gains in the worse eye from playing the video game binocularly. It is also likely critical to the demonstration of those gains during binocular post-tests. Not surprisingly, given the absense of binocular fusion, the patients showed no evidence of stereopsis on either the pre- or post-test. In contrast, the video game training study with strabismic and anisometropic amblyopes found substantial improvements in stereoacuity in all five anisometropic amblyopes who were studied (Li *et al.*, 2011). There may be more potential for such recovery in cases where there has always been coordinated binocular input to both eyes, even if the input to one eye was out of focus before treatment for anisometropia.

4.2. Changes in Higher-Level Vision

Deprivation amblyopia, like other forms of amblyopia, impairs not only low-level vision but also the perception of global form (Lewis *et al.*, 2002), of global motion (Constantinescu *et al.*, 2005; Ellemberg *et al.*, 2002), and of configural cues to face identity (Le Grand *et al.*, 2001, 2004), as well as selective visual attention (Goldberg *et al.*, 2001). Previous studies using video game training or perceptual learning with adults with strabismic or anisometropic amblyopia have not included any of these tasks. To assess whether the video game training also impacted these integrative skills that are critical to functional vision, we assessed sensitivity to global motion, to a configural face cue (feature spacing in upright faces), and the useful field of view with and without distractors.

Sensitivity to global motion was assessed with random dot kinematograms at two speeds — a relatively slow speed at which adults with normal vision have a relatively high coherence threshold (i.e., require a relatively high percentage of signal dots) and a faster speed to which they are more sensitive (i.e., require fewer signal dots to see the global direction). On the pre-test, patients typically required more than 50% signal dots for the slower speed and more than 25% for the faster speed — values far above normal. Although the monocular results were more scattered, most patients improved at both speeds on the binocular test.

Patients with bilateral deprivation amblyopia later have specific deficits in face processing, including deficits in using one of the cues central to adult expertise, namely, small metric differences between individual upright faces in the spacing of the internal facial features, a cue that has been called sensitivity to second-order relations (Le Grand *et al.*, 2001; Robbins *et al.*, 2010). Adults with normal vision are far less sensitive to second-order relations in inverted faces (e.g., Mondloch *et al.*, 2002). The pre-test confirmed the patients' deficit: they had virtually identical accuracy for upright and inverted faces (68 and 69%, respectively), such that their accuracy for upright was below normal (*cf.* 80% in normal adults) and their accuracy for inverted was within normal limits (*cf.* 70% in normal adults). After video game training, there was some evidence of increased sensitivity but no differential change for upright *versus* inverted faces. There may have been no change for face processing because, unlike the other tested skills, it had received practice with feedback during everyday interactions (e.g., embarassment after false recognition of a stranger) and thereby reached an asymptote. Medal of Honor also does not require accurate face recognition for successful playing.

Finally, we included a variant of the Useful Field of View (UFOV: Green and Bavelier, 2003; Sekuler and Ball, 1986) to test if patients can benefit from the training to improve in (1) speed of processing visual stimuli, (2) divided attention at eccentricities of 10°, 20°, and 30° and (3) selective attention (with or without distractors). Previous studies using other tasks indicate that patients with bilateral deprivation amblyopia are affected more than normal by distractors and do not uses cues normally to shift selective attention (Goldberg *et al.*, 2001). Despite such large scope for improvement, there was no improvement on the post-test in the minimum exposure time needed to detect peripheral targets or to avoid adverse effects of distractors. This contrasts with evidence that playing the same action video game (Medal of Honor) induces improvements in the useful field of view in adults with normal eyes (Green and Bavelier, 2003), as well as on another task requiring distributed attention (multiple object tracking) (Green and Bavelier, 2006a). The absence of improvement on this task, despite improvement, in at least some patients, on other tasks is surprising, especially given the demands of the game to monitor the entire field for events while ignoring unchanging attributes of the field. One clue to the lack of improvement is that, unlike the short critical period for damage to global motion, the critical period during which a period of visual deprivation can cause seemingly permanent deficits in peripheral vision extends into adolescence (Bowering *et al.*, 1997). Perhaps recovery from delayed visual input is also possible during that long period of plasticity and additional improvement is not possible thereafter.

4.3. Basis of Improvements

The success of this video game protocol in improving many aspects of vision indicates that there is enough residual plasticity in the visual system in adulthood, long after the end of the critical period for damage, to effect improvements even in cases of deep amblyopia caused by early bilateral deprivation. Animal models indicate that plasticity decreases during development because of structural brakes (e.g., formation of perineuronal nets) following interactions between sensory input and GABAergic inhibition (reviewed in Hensch, 2005) and that plasticity can be restored at least partially by removing the structural impediments (e.g., by chondroitinase ABC treatment) or decreasing GABAergic inhibition (e.g., by infusion with fluoxetine) (Pizzorusso *et al.*, 2006; Vetencourt *et al.*, 2008). Environmental enrichment in adult rats with monocular deprivation amblyopia appears to lead to improvements in acuity by effecting both types of change (Sale *et al.*, 2007). Video games might be effective because their stimulation of the worse eye helps to reset the excitatory/inhibitory balance and/or because playing the game effects neurochemical changes that decrease the structural brakes on plasticity.

Although the gains were modest in the present study and not evident for every aspect of vision tested nor in every patient, it is possible that performance would improve more with video game training that lasts longer than 40 h, a phenomenon that might parallel the small but continual improvements that have been shown to occur in perceptual learning tasks involving thousands of trials (Li *et al.*, 2008).

In summary, we found that training with an action video game for 40 h over 1 month is sufficient to improve many aspects of vision in adults with bilateral deprivation abmlyopia. The game may be effective because it contains the components of perceptual learning (stimulus/response/feedback) based simultaneously on many aspects of vision presented in a visually complex and challenging environment in an immersive, engaging, and adaptive way. Future studies are needed to identify the critical components of an effective game, the durability of the improvements, and whether greater gains can be effected if the game is combined with other interventions that are effective in enhancing plasticity of the adult brain (reviewed in Bavelier *et al.*, 2010).

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