Research report

Rapid compensation of visual search strategy in patients with chronic visual field defects

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\textbf{Article info}

\textbf{Article history:}
Received 9 April 2011
Reviewed 2 May 2011
Revised 7 March 2012
Accepted 28 March 2012
Action editor Giuseppe Vallar
Published online 20 April 2012

\section*{Key words:}
Hemianopia
Vision disorders
Rehabilitation
Eye movements

\textbf{Abstract}


text

\textbf{Introduction:}
The aim of this study was to test the effect and specificity of a novel, compensatory eye movement training therapy designed to improve visual search performance in patients with homonymous visual field defects.

\textbf{Methods:}
Seven patients with chronic homonymous visual field defects and six healthy control subjects were tested. All subjects completed the single training period (300 trials).

\textbf{Results:}
Pre-therapy we confirmed that patients differed from controls on the visual search task. Post-training we demonstrated a clear improvement in terms of reaction time required to complete the visual search. This effect was confined to: (1) the patient group only; (2) targets presented to the blind visual field of the patients only; (3) the visual search task only and not the rapid scanning or reading task.

\textbf{Conclusion:}
These results demonstrate that rapid, compensatory changes can occur in patients with visual field defects that impact on their ability to carry out efficient visual search. We plan to translate this therapy, along with appropriate testing materials, in a free-to-use, internet-based application based on this intervention.

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1. Introduction

Visual field deficits are common after acquired brain injury (Gilhotra et al., 2002). The majority of patients with unilateral post-chiasmatic brain damage exhibit a homonymous visual field defect, with posterior cerebral artery infarction being the most common cause (Zhang et al., 2006a; Zihl, 2011). Some spontaneous recovery can occur in roughly 40% of cases,
which is usually completed within the first 3 months after injury; improvements seen after 6 months are usually small in magnitude and considered to be due to improvement of the underlying disease (Zhang et al., 2006b). Thus, the majority of patients with acquired visual field defects are left with a visual impairment.

Despite this, some patients experience an improvement in visual function. This is most likely caused by spontaneous oculomotor compensation (compensatory eye movements that develop over time). However, most patients (at least 60%) continue to exhibit abnormal visual scanning behaviour with increased reaction times on visual search tasks (Zihl, 1995a).

This partly explains why patients with persistent visual field defects often report difficulty in carrying out activities of daily living (Han et al., 2002; Warren, 2009), with the presence of a homonymous hemianopia being a powerful negative predictor of a patient’s outcome, even on crude measures such as discharge to own home following a stroke (Friedman, 1995; Gray et al., 1989; Reding and Potes, 1988; Patel et al., 2000).

There are currently three main approaches to rehabilitation of visual field defects and they all have one therapeutic principle in common: mass practice of a specific visual task, with the expectation that improvement on this task will generalize to a range of ecologically useful visual functions. The available treatments aim to: (1) replace part of the intact visual field with part of the damaged field (optical therapy e.g., using prisms); (2) partially restore the lost visual field region (restorative therapies); (3) compensation by reorganizing the process of making exploratory eye movements into the blind field (compensatory therapies) (Schofield and Leff, 2009). The compensatory therapies appear to have the most therapeutic promise in terms of the ratio of behavioural improvement to hours of practice. Indeed, behavioural improvements have been reported at the group level after as little as 7 h of practice (Schuett, 2009). This contrasts starkly with restorative therapies which require tens of thousands of trials over many weeks or months to significantly improve sensitivity to targets deep in the blind field (Sahraie et al., 2006).

The motivation for this proof-of-principle study was to investigate whether this effect could be reproduced in a single therapy session lasting approximately 30 min. Crucially, the main outcome measure was not whether the patients improved their speed or accuracy on the therapy task itself (Nelles et al., 2001; Pambakian et al., 2004), or on a task requiring detection of abstract shapes (Bolognini et al., 2005), but on a ‘real world’ visual search task (Keller and Lefin-Rank, 2010). This is important because rehabilitation techniques that rely on mass practice of a task that has no ecological validity in itself (as is the case in this study) must be shown to have carry-over effects to environments that patients frequently encounter, if they are to have any claims on usefully changing behaviour. Another option is to look for training effects on more remote functional outcomes, such as activities of daily living that are known to be commonly impaired in patients with hemianopia (Warren, 2009). This is an important aspect for rehabilitation in general but does not apply to this proof-of-concept study as our aim was to investigate whether it might be possible to observed significant improvements in visual function in a single day’s therapy; changes in functional outcomes require considerably longer periods.

We included a group of healthy, age-matched subjects to control for practice effects. We also included two outcome measures that depend on different aspects of visual function to investigate the specificity of any carry over that the ramp-step therapy may have had. First, we used text reading which also depends on voluntary saccades, but reading saccades have a very different pattern to visual search saccades, reflecting the different cognitive processes underlying the two tasks. Saccadic retraining therapy for reading has been shown to depend on using certain types of visual stimuli, namely those that require stimulus-driven induction of, or voluntary production of, small amplitude saccades (Schuett et al., 2008; Spitzyna et al., 2007). Second, we used a ‘pop-out’ search task where the target’s location can be rapidly identified because it differs from the background so much that it can be detected by parafoveal/peripheral vision in a rapid scanning task (Saarinen, 1996).

## 2. Methods

### 2.1. Subjects

Six healthy subjects (Controls C) with normal or corrected-to-normal vision and seven patients (P) with chronic visual field defects participated in the study [mean age = 58.9 years (±15.6 SD)]. Subjects gave informed consent to participate according to the Declaration of Helsinki. Patients were recruited from the General Neurology clinic at National Hospital for Neurology and Neurosurgery, and all procedures were approved by the Hospital Ethics Committee. Patient selection was based on availability of visual perimetry. The patients had suffered unilateral lesions in either the right or the left posterior hemisphere and were in the chronic phase post-injury [mean time post-injury = 2.9 years (±2.5)]. Patients showed a normal or corrected-to-normal binocular visual acuity for near and far vision. All patients were examined clinically by a neurologist and were excluded from the study if they had: glaucoma, an abnormality of ocular mobility or neglect. Four patients exhibited a right visual field defect (P,RH) and three patients a left deficit (P,LH). Individual details concerning sex, age, length of illness, lesion sites, aetiology and the presence of visual field defect are reported in Table 1. We define macular sparing as ±1–5°.

### 2.2. Examination of scanning abilities: pre- and post-tests

All subjects (Controls and Patients) underwent examination of their visuo-motor scanning abilities with three different tasks (a visual search task of a complex and crowded scene, a rapid scanning task with easily-detectable targets, -so-called ‘pop-out’ items-, and a standard text reading task). Three evaluation sessions were performed, two before (Pre1 and Pre2) and one immediately after the training period (Post). The three evaluation sessions along with the training procedure occurred on the same day. Subjects had a short rest period between each session and training procedure. The time
interval between the two-pre-evaluations corresponds to a short rest period of 10 to 15 min. The training session was about 30 min long. Duration of the whole procedure (evaluation and training) did not exceed 3 h.

Subjects were seated comfortably in front of a computer monitor with their head supported by a chinrest to reduce the effect of head movements.

2.2.1. Visual search

The aim of this task was to simulate an ecologically valid test of visual search where subjects had to search for an everyday object in a crowded desk scene. Each trial began with presentation of a target object for 5 sec in the middle of the screen. This was then replaced by an image of a cluttered desk (example in Fig. 2, inset), and the subject was instructed to search within this image for the target item. Crucially, on approximately half the trials the object was not present in the scene. Subjects used a button press to indicate when they had completed the search, either because the item was found or they had determined it was not present. Subjects then indicated verbally whether the target was found or not. We measured the reaction time (msec) from onset of the desk image to when the subject terminated the search. Errors were also recorded. Each session included 13 trials (seven with target object present, six with target object absent). Different images were used for each session. For patients, target-present trials were analyzed separately depending on whether the target was on the intact or impaired side.

2.2.2. Rapid scanning task

Search arrays consisting of 24 green squares (evenly-distributed in a 4 × 6 arrangement) were presented in rapid sequence (2 sec per array, 250 msec interval). In each array, a target (red letter) was displayed in a randomly-chosen square. The subject was instructed to locate each letter as quickly as possible, and to press the response button only when they saw the letter 'X' (50% of arrays, with equivalent distribution between left, right, top and bottom quadrants). Again, reaction time and errors were measured. Each session consisted of 96 presentations. A different sequence of arrays was used for each session.

2.2.3. Reading task

A standard paragraph with seven lines of text (Times New Roman, 20 pt) was presented on the screen. Subjects were asked to, “Please read silently at a comfortable speed.” Each session included four paragraphs, with new text used for each session. Subjects were asked after each session to briefly report the main topic of their reading, to assure a global or gist level of understanding. Reading speeds (words per minute) were calculated by dividing the number of words in each paragraph by the reading time.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Lesion</th>
<th>Aetiology</th>
<th>Delay (years)</th>
<th>Visual field defect</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>68</td>
<td>L parieto-occipital</td>
<td>Stroke</td>
<td>8</td>
<td>RupQ, no macula sparing</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>66</td>
<td>L infero-medial occipital</td>
<td>Stroke</td>
<td>3</td>
<td>RH, macula sparing</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>38</td>
<td>L occipital</td>
<td>Post-surgical tumour</td>
<td>4</td>
<td>RH, no macula sparing</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>41</td>
<td>L temporo-occipital</td>
<td>Post-surgical tumour</td>
<td>1</td>
<td>RH, macula sparing</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>77</td>
<td>R occipital</td>
<td>Stroke</td>
<td>1</td>
<td>L, lower Q, macula sparing</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>72</td>
<td>R occipital</td>
<td>Stroke</td>
<td>2</td>
<td>LH, no macula sparing</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>50</td>
<td>R occipito-parietal</td>
<td>Stroke</td>
<td>1</td>
<td>LH, no macula sparing</td>
</tr>
</tbody>
</table>

H: Hemianopia; Q: Quadransopia [upper or lower]. Macular sparing was defined as ±1°–5°.

Fig. 1 — (a) Computer-screen display – a stimulus is crossing the screen from left to right or right to left (here, from left to right); – subject had to pursue the stimulus (ramp phase) and then saccade to find its location when it suddenly jumped (step phase); – at the place where it reappeared, the gap of the stimulus could be located at either the top (50%) or at the bottom (50%), and patients had to indicate this using a response button as quickly as possible. (b) Velocity profile of the target – ramp phase means constant velocity before the sudden step.
2.3. Training procedure

The computer-based training task consisted of a novel ramp-step search paradigm, in which subjects had to pursue a smoothly-moving stimulus (ramp phase) from one side of the display to the midline, and then generate a saccade to its new location when it abruptly jumped into the opposite hemifield (step phase).

On each trial, the target stimulus (a black letter C within a white disc, see Fig. 1) initially appeared at a horizontal position deviated by 17.5° of visual angle from the midline, either to the right or left (on alternate trials). The target then began to ‘roll’ towards the midline at a constant velocity of 15°/s and with a randomly-chosen trajectory between 20° above and 20° below the horizontal. After translating a randomly-selected distance between 15° and 20°, the target abruptly jumped a further 15° along the same trajectory. Subjects were instructed to follow the target to its final location, and then indicate as quickly as possible with a response button whether the gap in the letter C was at the top (50% of trials) or the bottom (50%) of the target. The speeded response requirement encouraged subjects to fixate the whole translation of the stimulus in order to predict the trajectory of the subsequent jump (see Fig. 1).

The training task was split into three sessions of 100 trials each, separated by brief rest breaks. Each session lasted roughly 8 min, and the training procedure as a whole took approximately 30 min. Reaction times were measured, as well as errors. Trials on which subjects responded incorrectly were excluded from further analysis.

2.4. Statistical analysis

We performed ANOVAs with group as the between-subject factor (C = control, P = patient) and session (Pre1, Pre2, Post) as the main within-subject factor. For each test we first examined the test–retest reliability by comparing data at Pre1 with Pre2; we then looked for treatment effects by comparing an average of the Pre-data with the Post-data. Further comparisons of the means were used when appropriate. Threshold for statistical significance was set at \( p < 0.05 \).
3. Results

3.1. Visual search task ‘Desktop task’

The visual search task is not a standard test so we wished to assess its test–retest validity and also establish that controls and patients performed differently on it, prior to using it to investigate therapy-induced changes in visual search.

3.1.1. Validity

A $2 \times 3 \times 2$ ANOVA was performed with session (Pre1 Pre2) and Condition (Object Absent Object Present) as within-subject factor and group (C P) as between-subject factor.

Firstly there was no Session effect (F(1,10) = 0.26; p > 0.6), suggesting that the test has a robust test-retest profile. Secondly there was a difference between P and C (F(1,10) = 19.26; p < 0.002), patients (P = 10,336.9 msec ± 682 SE) being slower than controls (C = 5698.5 msec ± 807 SE), suggesting that the test can differentiate between groups. Lastly, there was also a condition effect [F(2,20) = 5.80; p < 0.02], with both groups being slower when looking for absent target (Abs = 10,637.11 msec ± 1409 SE) than looking for present target (in the intact visual field Preintact = 6238.45 msec ± 1243 SE as in the blind visual field Prehemi = 7177.51 msec ± 1359 SE).

3.1.2. Effect of intervention

We then used the task to test the effects of the intervention. We compared performance between the pre-test condition (average performance on both pre-tests) and the post-test condition, for each group, A $2 \times 3 \times 2$ ANOVA was performed with session (Pre Post) and Condition (Object Absent Object Present (Hemi) intact Object Preintact Object Prehemi) as within-subject factor and group (C P) as between-subject factor.

We found: (1) an effect of group (F(1,10) = 12.30; p < 0.006), with patients (P = 9192.9 msec ± 660 SE) being slower than controls (C = 5540.8 msec ± 782 SE). (2) A condition effect [F(2,20) = 18.65; p < 0.0005], with both groups being slower when looking for an absent target (Abs = 10,431.67 msec ± 1352 SE) than when looking for a present target (whether in the intact visual field Preintact = 5727.62 msec ± 709 SE, or in the blind visual field Prehemi = 5846.71 msec ± 884 SE). (3) A session effect [F(1,10) = 8.89; p < 0.02], with reaction time being faster after the therapeutic intervention (Post - = 6652.98 msec ± 1023 SE) than before (Pre = 8017.7 msec ± 915 SE), but, importantly, with a significant session × group interaction [F(1,10) = 5.28; p < 0.05] (CPre = 5698.49 msec ± 1398 SE; CPost = 5383.14 msec ± 1563 SE; Ppre = 10,336.90 msec ± 1182 SE; Ppost = 7922.82 msec ± 1321 SE). Planned comparisons were performed to specify which group improved. The Pre/Post comparison for the Control group was not significant [F(1,10) = 0.20; p = 0.66], whereas the Pre/Post comparison for the Patient group was significant [F(1,10) = 16.70; p < 0.003] (Fig. 2). In addition, there was no condition × group, condition × session nor three way interaction (Fs < 1.2; ps > 0.3).

3.1.3. Omissions

Mean omissions rate (1% of correct responses) was analyzed first in the pre-tests conditions. A $2 \times 2$ ANOVA was performed with session (Pre1 Pre2) as within subject and group (C P) as between subject. It showed a group effect [F(1,10) = 4.98; p < 0.05], with patients (P = 15.9% ± 3.1 SE) making more omissions than controls (C = 5.4% ± 3.6 SE). There was no session effect nor a session × group interaction (Fs < 1.4; ps > 0.2). When looking at the differences between intact and affected hemifield, patients showed higher omission rate in the blind visual field (17.6% ± 5.2 SE) compared to the intact one (14.3% ± 5.5 SE). Interestingly, right-hemianopic patients showed evident asymmetry in omission rate (Intact = 1.9% ± 3.5 SE; Blind = 21.2% ± 5.4 SE), while left-hemianopic patients exhibited unexpected reverse pattern (Intact = 30.8% ± 6.1 SE; Blind = 12.8% ± 8.5 SE).

The Pre–Post comparison $2 \times 2 \times 2$ ANOVA with session (Pre Post) and condition (Intact Hemi) as within-subject factor and group (C P) as between-subject factor showed only a session effect [F(1,10) = 16.97; p < 0.002], with less omissions after training (4.8% ± 4.0 SE) than before (13.4% ± 3.9 SE). There was no group nor condition effect nor two way or three way interactions (Fs < 0.69; ps > 0.42).

3.2. Rapid scanning task

3.2.1. Reaction time

As with the previous task, we first wished to establish that there were no significant test–retest effects. A $2 \times 2 \times 2$ ANOVA with session (Pre1 Pre2) and condition (Intact Hemi) as within-subject factor and group (C P) as between-subject factor was therefore performed. We found no difference between the two pre-test sessions (no group effect [F(1,10) = 3.24; p > 0.10]; no condition effect [F(1,10) = 0.54; p > 0.47]; no session effect [F(1,10) = 0.80; p > 0.12]); nor condition × group, session × group or three way interaction (Fs < 2.9; ps > 0.12).

We then compared the performances between the pre-test condition (average performance on pre-tests) and the post-test condition, for each group, A $2 \times 2 \times 2$ ANOVA with session (Pre Post) and condition (Intact Hemi) as within-subject factors and group (C P) as between-subject factor was performed.

We found no group effect [F(1,10) = 3.48; p > 0.09], nor session effect [F(1,10) = 2.58; p > 0.13]; however, we did find a condition effect [F(1,11) = 5.01; p < 0.05], with patients being slower on their hemianopic side (Pre = 1271.2 msec ± 365 SE; Post = 1218.7 msec ± 330 SE) compared with the intact field (Pre = 1102.1 msec ± 269 SE; Post = 1084.5 msec ± 302 SE). No session × group, condition × group nor three way interaction was found (Fs < 2.59; ps > 0.13).

3.2.2. Omissions

Mean omissions rate (1% of correct responses) was first analyzed in the pre-test conditions. A $2 \times 2$ ANOVA with session (Pre1 Pre2) as within-subject and group (C P) as between-subject factors was performed. It showed a borderline significant group effect [F(1,10) = 4.58; p = 0.06], with patients (P = 6.5% ± 2.1 SE) making more omissions than controls (C = 0% ± 2.2 SE). There was no session effect nor session × group interaction (Fs < 0.24; ps > 0.6).

When looking at the differences between intact and affected hemifield, patients showed higher omission rate in
the blind visual field (9.8% ± 3.3 SE) compared with the intact one (3.1% ± 0.9 SE).

Again we looked for therapy effects using a 2 × 2 ANOVA with session (Pre vs. Post) and condition (Intact Hemianopic vs. Within-subject factors) and group (C vs. P) as the between-subject factor. This showed only a group effect \(F(1,10) = 4.90; p < 0.05\), with patients showing higher omission rate compared to the control group. There was no session nor condition effect nor two ways or three way interactions (\(Fs < 5.8; ps > 0.05\)).

3.3. Reading task

Once more, we wished to establish test–retest reliability first. A 2 × 2 ANOVA with session (Pre1 vs. Pre2) as within-subject factor and group (C vs. P) as between-subject factor was therefore performed. There was no session effect nor session × group interactions (\(Fs < 2.32; ps > 0.15\)).

We did find a borderline significant group effect \(F(1,10) = 4.73; p = 0.06\), with patients (117.9 wpm ± 23 SE) being slower than controls (196.4 wpm ± 28 SE). This appeared to be driven by the patients with right-sided hemianopias as these patients are usually more impaired on text reading than those with left-sided hemianopia (Zihl, 1995b).

To look for any therapy effects, we compared performance between the pre-test (average performance on pre-tests) and the post-test condition. There was a significant group effect \(F(1,10) = 4.75; p = 0.05\), with a significant session effect \(F(1,10) = 5.93; p < 0.04\), reading speed being faster after treatment (167.2 wpm ± 20 SE) compared to before (157.2 wpm ± 18 SE). Importantly, there was no group × session interaction \(F(1,10) = 1.56; p > 0.24\), both groups having improved.

4. Discussion

The main objective of this proof-of-concept study was to investigate whether a compensatory eye movement training therapy, using a novel ramp-step paradigm, could improve hemianopic patients’ visual search on a real-world task after only one session of therapy (300 trials). Before therapy, patients were significantly impaired, compared to controls, on both visual search and rapid scanning tasks, with longer reaction times in particular on the hemianopic side. After training a clear improvement in RTs was demonstrated in the visual search task in the patients’ group. Importantly, this was confined to the blind visual field only, with no ‘cost’ or worsening of performance in the unaffected visual field. Interestingly, the improvement was only observed in the cases where targets were present. When the targets are absent reaction times are longer probably because subjects have to search longer before responding. This condition is probably affected by conscious strategies that have been overlearnt. It is possible that, due to their long-standing hemianopia, the patients have adopted a cautious approach to accepting an item is absent. One would perhaps not expect this to improve in a single session, but perhaps after many sessions, when they have updated their prior expectations of their more efficient scanning behaviour, it would.

Patients improved on the visual search task significantly compared to controls suggesting that this effect was not due to a practice effect on the visual search task. Moreover, there was no significant change over the two baseline assessment sessions (Pre1 and Pre2), so patients’ performances were steady before the eye movement training intervention, improved after it, but still remained slower than controls'. Thus we conclude that the alteration in performance on the desktop search task is most likely due to patients performing the eye movement training task. However, it will be important in future studies to see if this effect can be replicated in other patients. No treatment effects were observed in the rapid scanning task, suggesting that the therapy was task-specific. In the reading task, a significant improvement was observed, however, this affected both groups (there was no group by condition interaction as in the search task) this may have been due to a general learning effect on our stimuli.

The generalizability of any rehabilitation therapy that is based on mass practice is very important. Too much specificity and the potential benefits to the patient reduce, especially if the therapy task is non-ecological, as is almost always the case in therapy for patients with visual field defects. A lack of any specificity calls into question the mechanism of improvement on the test tasks. If patients improve their performance on every outcome measure then perhaps the observed effect is due to practice effects on the outcome tasks. A recent study using cross-modal (audio-visual) therapy to improve compensatory eye movements in hemianopic patients, demonstrated a significant effect of therapy on all outcome measures, including text reading (Keller and Lefin-Rank, 2010), suggesting that there may have been some non-specific therapy effects. An important, recently published study has a direct bearing on this question. Schuett et al. (2012) investigated the specificity of eye movement therapy for patients with hemianopia using a cross-over design. They found that therapy that improved visual search performance did not carry over to affect reading speeds, and, vice-versa: therapy that improved reading speed did not carry over to affect visual search (Schuett et al., 2012), probably because the two therapies induce different types of eye-movements in terms of saccadic amplitude and angle.

Such a result is difficult to understand in terms of saccadic mechanisms as the training was to targets positioned in 8° steps away from fixation, yet in text reading the average saccadic amplitude is in the region of 1–2° (Ducrot and Pynte, 2002). A potential way to try and control for this type of effect is to have a placebo therapy group, but this is rare in behavioural therapy studies in general, and certainly for studies of patients with hemianopia, although there are exceptions (Spitzyna et al., 2007). The therapy effects seen in this study, admittedly on a small group of patients, were specific to the type of eye movements used in visual search, but not to those used in text reading or rapid scanning, supporting the inference that the improvement in visual search was indeed due to a therapy-induced change in behaviour.

These results are encouraging with respect to promoting compensatory rehabilitation for patients with visual field defects that impact on their ability to carry out efficient visual search. An important consideration, which we have not addressed in this proof-of-principle study, is the duration of
any beneficial effects. Will these gains remain static or require continued, intermittent practice with the therapy materials to endure? Also, what is the best way to deliver this type of therapy? One option that may help solve both of these important questions is to use the internet to both deliver the therapeutic material and record its effect on basic, ecologically valid, tests of visual function. This is currently ongoing for a specific reading disorder caused by hemianopia (hemianopic alexia): http://www.readright.ucl.ac.uk/. We are currently developing a similar free-to-use application that will deliver the ramp-step therapy described here (http://www.eyesearch.ucl.ac.uk).

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