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# Computer based vision restoration therapy in glaucoma patients: A small open pilot study

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**Abstract**. *Purpose*: Several studies have shown that computer-based visual stimulation improves detection performance in brain damaged patients with post-chiasmatic lesions after stroke or trauma. Because it is not known whether visual field defects after retinal lesions can also be modified by visual stimulation we explored if visual field enlargements are possible in patients with glaucoma.
*Methods*: Five patients with primary open angle glaucoma (POAG) performed Vision Restoration Training (VRT), a computer-based vision training for a total of 6 months in two 3-months blocks with a 3-months training-free interval between the two training periods. Perimetric testing was performed with High Resolution Perimetry (HRP) as well as with 30° and 70° white/white (W/W) and 30° blue/yellow (B/Y) conventional automatic perimetry (Oculus Twinfield).
*Results*: After the first 3 months of training the average detection performance significantly increased in HRP ($Z = -2.023$, $p < 0.05$) and in 30° W/W perimetry ($Z = -2.023$, $p < 0.05$), but not in B/Y perimetry ($Z = -1.214$, $p = 0.225$) or in the 70° W/W perimetry, which included more peripheral, non-trained areas ($Z = -0.406$, $p = 0.684$). Visual improvements remained stable after the training-free interval. Measured by HRP after the second VRT period 3 patients achieved an increase in the ability to detect visual stimuli, however, this improvement did not reach significance ($Z = -1.826$, $p = 0.068$).
*Conclusions*: While a small patient sample does not permit general conclusions on visual field recovery after glaucoma, this pilot study suggests that visual field defects caused by retinal lesion may be improved by systematic vision stimulation. A larger sample, randomized clinical trial is now warranted.

Keywords: Glaucoma, visual field, visual field stimulation, visual field recovery

## 1. Introduction

Glaucoma is an optic neuropathy characterized by a gradual loss of the retinal nerve fiber layer and ganglion cell death with consequent damage to the optic nerve. This structural damage is predominantly caused by elevated intraocular pressure (IOP). If not detected early, glaucoma produces permanent vision loss as evident by visual field defects. The treatment of glaucoma aims at limiting or preventing its progression by a reduction of IOP using drugs, laser treatment, or incisional surgery (Coleman, 1999). While the ultimate goal is to arrest further neural damage and visual field deterioration, no attempt has yet been made to restore the lost visual functions because it is believed that such visual field defects are permanent.

Since a few retinal ganglion cells survive within the damaged retinal region (Pavlidis et al., 2003; Villegaz-Perez et al., 1993) and the deafferented visual cortex shows significant plasticity of receptive field size and location (Chino, 1999; Eysel et al., 1999; Gilbert & Wiesel, 1992), both mechanisms may provide a neu-

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ronal substrate for restoration of some useful visual functions after retinal lesion. Evidence for spontaneous and training induced recovery from visual field defects in brain damaged patients has been reported in several studies (Julkunen et al., 2003; Kasten & Sabel, 1995; Kasten et al., 1998; Kerkhoff et al., 1994; Messing & Gänshirt, 1987; Mueller et al., 2006; Mueller et al., 2007; Poggel et al., 2001; Potthoff, 1995; Zhang et al., 2006). Specifically, we have proposed that residual neurons surviving partial damage in brain regions after stroke or brain damage might provide the biological substrate for significant restoration potential. Vision Restoration Training (VRT) has been used for many years in brain-damaged patients achieving both visual field enlargements (Kasten & Sabel, 1995; Kasten et al., 1998) and reaction time gains which lead to improvements of subjective vision (Mueller et al., 2003; Sabel et al., 2004). These changes are not a consequence of eye movement behavior (Kasten et al., 2006; Sabel et al., 2004).

The goal of the present pilot-study was to explore if functional restoration is possible in the visual system of patients with visual field defects due to retinal lesion caused by glaucoma. We were particularly encouraged to explore this possibility for various reasons: (i) VRT has been shown to be more effective in patients with optic nerve damage (Kasten et al., 1998), (ii) in single patients with anterior ischemic optic neuritis (AION) improved light detection was found after VRT (Mueller et al., 2007; Jung et al., 2008), and (iii) the visual system's plasticity likely involves receptive field reorganization in the deafferented visual cortex (Gilbert & Wiesel, 1992).

## 2. Methods

### *2.1. Patients*

The study was planned as an exploratory, open, pilot trial with a small number of patients ($n = 5$). The patients (1 woman, 4 men) were 55–81 years old ($65.4 \pm 9.71$ years, mean $\pm$ SD) and they had been diagnosed by their ophthalmologist as suffering from primary open angle glaucoma (POAG). Patient sample characteristics are described in Table 1. All patients had reproducible visual field defects and were on continuous drug treatment to lower and stabilize their intra-ocular pressure (IOP). Three patients had binocular and two patients monocular glaucoma. Prior to study entry, patients had been excluded if at least one of the following exclusion criteria applied: unstable visual field (significant fluctuation), presence of any chronic-degenerative disease of the nervous system (e.g. senile/pre-senile dementia), severe cognitive impairments (e.g. attentional deficits), motor disturbances (e.g. hemiplegia), neglect, nystagmus or other forms of impairments to fixate, amblyopia, photosensitivity, history of trauma, any other ocular diseases (e.g. diabetic retinopathy) or ocular surgery at least one year prior to recruitment or expected ocular surgery within the six months after study entry. Participation in the study required informed consent by the patients. Patients received detailed information about the purpose, organization and risks of the study. The patients were thus well aware of the purpose of the study and none of the patients underwent a control (placebo) condition. Furthermore, patients were instructed to continue with any medical treatment they might be receiving from their attending ophthalmologist.

VRT was performed over a period of two 3-months sessions for $2 \times 30$ minutes daily. To determine the stability of VRT-induced visual field changes there was a 3-months training-free interval between the two training periods (ABA design, where A = VRT and B = non-treatment period). Patients underwent standardized examination of their visual field before commencing with VRT (baseline assessment), after 3-months of VRT (Post 1), after a training-free phase at 6 months follow-up (Follow-up) and after an additional 3-months VRT interval, i.e. at 9 months (Post 2). One patient discontinued the training after the follow up examinations due to a heart attack. Consequently, four out of five patients completed the second VRT period.

### *2.2. Baseline assessments*

The visual field was tested with different methods of quantitative perimetry: monocular standard white-on-white (W/W) and blue-on-yellow (B/Y) perimetry as well as high-resolution perimetry (HRP). Both W/W and B/Y perimetry were performed using the Twinfield Perimeter (Oculus, Model 56900). Since it is well recognized that glaucoma patients experience fluctuations in their visual fields (Heijl et al., 1989; Hutchings et al., 2001; Werner et al., 1989), we first established a stable baseline with six repeated visual field examinations (three times in the morning, three times in the afternoon) using super-threshold HRP field tests (description see below). These were applied at six different sessions throughout a time window of 6–10 weeks. These six visual field tests also served to determine areas of residual vision (ARVs) as previously described

Table 1
Patients' demographic and medical data

| Patient | Sex | Age | Type of Glaucoma | Affected Eye(s) | Trained Eye(s) | Date of Diagnosis | Mean IOP (Hgmm) | CDR | Medication |
|---|---|---|---|---|---|---|---|---|---|
| **A** | f | 62 | POAG | OD | OD | 2000 | OD 16 | OD 0.6 | Dorzolamide |
| | | | | | | | OS 16 | OS $< 0.5$ | |
| **B** | m | 81 | POAG | both | OD | 2000 | OD 12 | OD 0.5 | Dorzolamide |
| | | | | | | | OS 12 | OS 0.5 | |
| **C** | m | 62 | POAG | OS | OS | 1998 | OD 16 | OD 0.6 | Dorzolamide |
| | | | | | | | OS 16 | OS 0.7 | Latanoprost |
| **D** | m | 55 | POAG | both | OD | 1992 | OD 15 | OD $< 0.5$ | Brinzolamide |
| | | | | | | | OS 15 | OS $< 0.5$ | Timolol |
| **E** | m | 67 | POAG | both | OD | 1972 | OD 15 | OD 0.9 | Brinzolamide Bimatoprost |
| | | | | | | | OS 15 | OS 0.9 | |

Note: f = female, m = male, POAG = Primary Open Angle Glaucoma, OD = right eye, OS = left eye.

(Kasten & Sabel, 1995) which were then used to establish each patient's individual training program. After each training unit of 28 days, control diagnostic examinations were carried out using HRP as well. On the basis of these HRP diagnostic results and training results, training parameters were adjusted based on the patient's training progress. In addition to the visual field tests, each patient was evaluated for medical history and examined for visual acuity using the Landolt C-test (Haas & Hohmann, 1982) and for contrast sensitivity evaluation using the Functional Acuity Contrast Test (Ginsburg, 1984). In an oral interview before and after training respectively, patients were also asked whether they had noticed visual impairments due to glaucoma in everyday life and whether they experienced positive effects of VRT. Moreover, the patients were examined on a regular basis by the attending ophthalmologist and were well controlled on medical therapy throughout the study. None of the patients changed their own individual drug treatment protocol over the course of the study.

### 2.3. Oculus automatic perimetry

We employed the Oculus automatic threshold oriented perimetry to determine visual field size. Testing was performed monocularly with static light stimuli within $30^\circ$ and $70^\circ$ of visual angle using 188 and 97 stimuli, respectively. The $30^\circ$ visual fields were examined with white light stimuli (stimulus size: Goldmann III, presentation time: 200 ms, interval time: 600 ms) on a white background (background luminance: 10 cd/m$^2$). For the blue-on-yellow perimetry, the blue light stimulus size was Goldmann III, presentation time: 200 ms, interval time: 600 ms, on yellow background (background luminance: 100 cd/m$^2$). The B/Y perimetry was deemed to be a particularly sensitive measure since it measures short-wavelength sensitivity mechanisms (the SWS channel) and is more effective than W/W perimetry in detecting early glaucomatous visual field defects (Bayer & Erb, 2002; Johnson et al., 1993). Fixation was controlled by a video camera. Furthermore, positive catch trials were obtained in all examinations.

### 2.4. High resolution perimetry (HRP)

The High Resolution Perimetry is a computer-based campimetric procedure for assessment of the central visual field ($\pm$ 27° horizontal and $\pm$ 20° vertical eccentricity). Validity and reliability of the method was ascertained in an earlier study (Kasten et al., 1997). The patient sits in front of a 17″ computer monitor and the head is stabilized with a chin rest. On a dark screen (luminance 20 cd/m$^2$) white target stimuli (luminance 83 cd/m$^2$) are presented for 150 ms in random order at 474 different positions in a grid of 25 $\times$ 19 stimulus locations. The patient has to keep his/her eyes on the fixation point throughout the test and is instructed to hit the space-bar on the computer keyboard whenever a target stimulus is presented or the fixation point changes its colour from bright green to bright yellow. In addition, fixation is controlled by the experimenter observing the patient's eye position in a mirror. The number of hits, false hits, misses and reaction times are recorded automatically by the program. Visual field testing was carried out without eye-glasses.

### 2.5. Vision restoration training (VRT)

The computer-based Vision Restoration Training (VRT) is a neuropsychological method which has been described repeatedly (Kasten & Sabel, 1995; Kasten et al., 1997; Kasten et al., 1998). The basic principle of VRT is that by regularly stimulating areas of residual

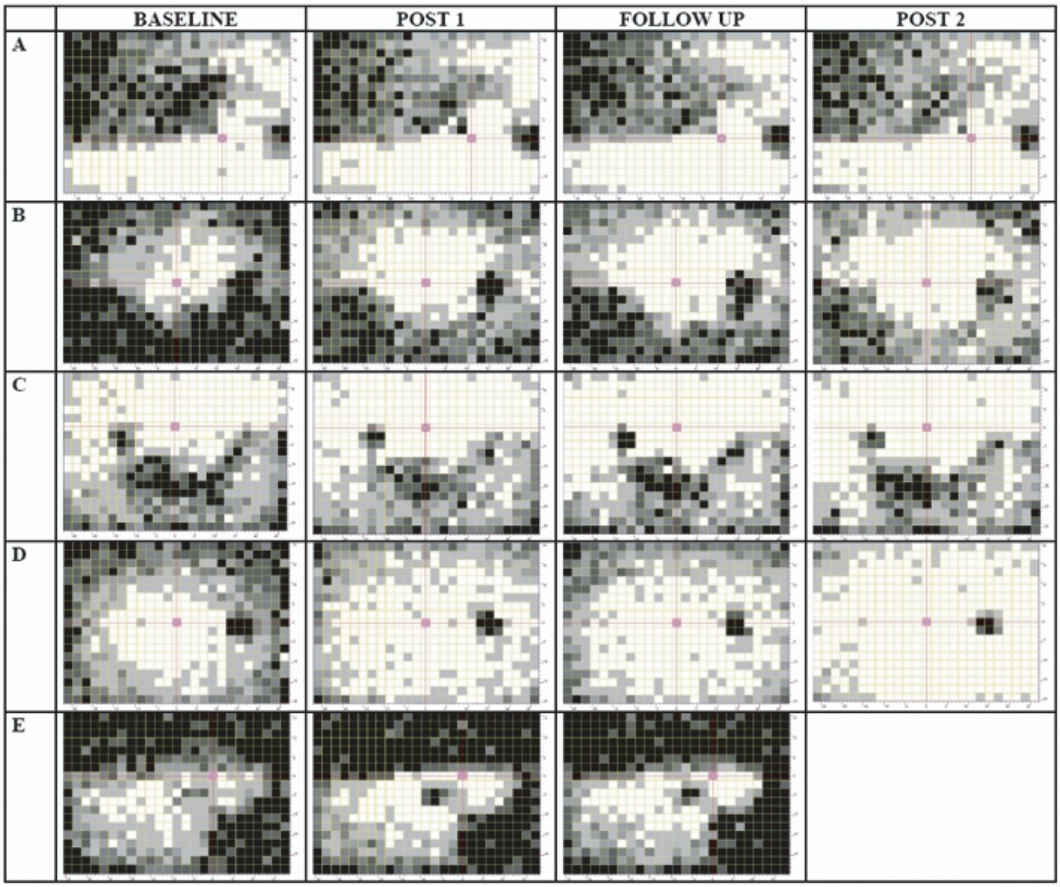


Fig. 1. Superimposed HRP (6 measurements) visual field test results for all patients measured at baseline, after the first 3-months VRT period (post 1), after subsequent 3-months follow-up without training (FU) and after the additional 3-months VRT phase (post2). Patient E discontinued the training after the follow up examinations therefore just baseline, post 1 and follow up results are presented. In HRP grey areas represent regions where stimuli are detected only sometimes (between 1–5 times), the black areas the blind visual field and the white areas the intact visual field. Patient A and patient C showed a moderate improvement after 6-months VRT (7.68% and 7.41%, respectively). The visual field of patient B and patient D changed remarkably after 6-months of training (34.31% and 39.4%, respectively). In case of patient E the level of stimulus detection remained constant.

vision through training, plasticity of the visual system is induced. The program projects white light stimuli on a grey background into areas with residual visual function. The patient has to press a key on the keyboard whenever he or she detects the presented stimuli. VRT was carried out monocularly. If both eyes were suitable for training (i.e. showing visual field defects with identifiable areas of residual vision) the dominant eye was chosen.

## 3. Data analysis

Statistical analysis was performed using SPSS 10. Wilcoxon-test was calculated for group analysis and comparison of pre – post 1, post 1 – post 2 and post 1 – follow up VRT differences, respectively. Note that for the comparison of post 1 – post 2 training results we only included data obtained in four patients because one patient dropped out (see above). Both HRP and perimetric data analyses were based on the number of hits (detected /recognized stimuli). In case of the perimetric data, relative defects, i.e. positions in the visual field with a decreased light sensitivity, were defined to be “stimulus detections”. The level of significance was set at an alpha of $p < 0.05$.

## 4. Results

This section focuses on the general effect of VRT on the complete patient sample and on the description

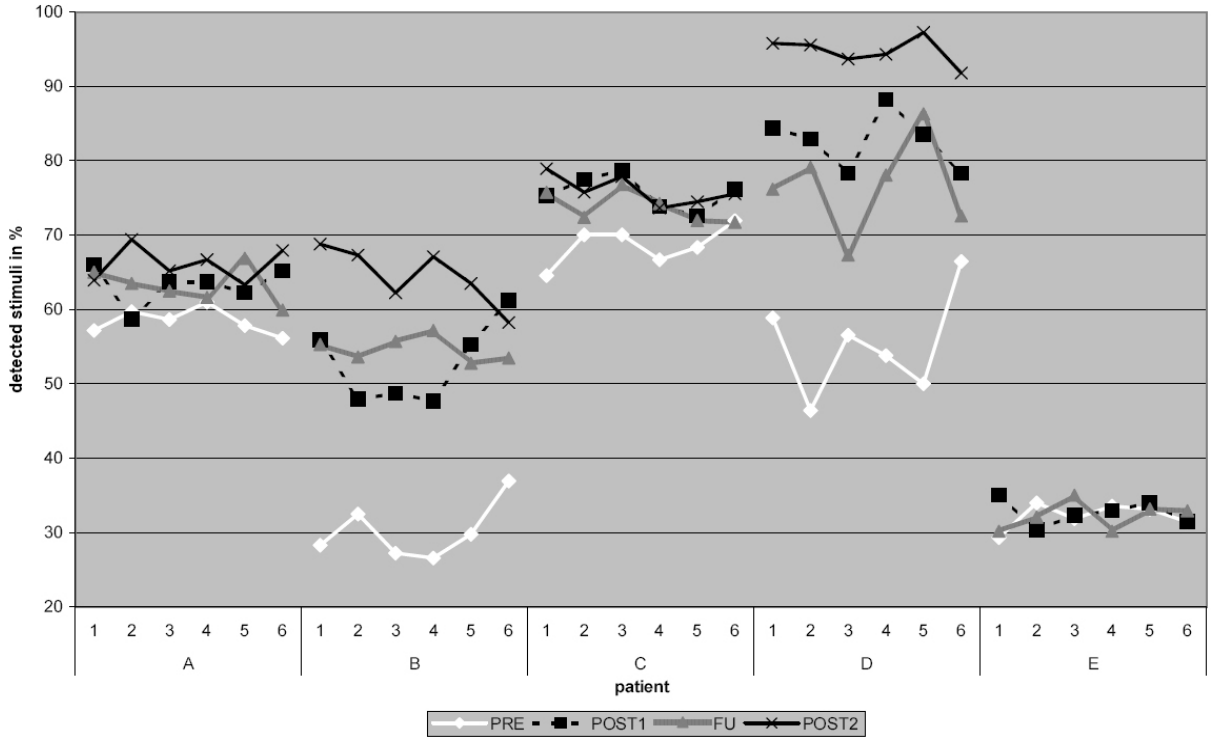


Fig. 2. Stimulus detection rate (in %) in the 6 HRP visual field tests measured at baseline (pre), after the first 3-months VRT period (post 1), after subsequent 3-months follow-up (fu) and after the additional 3-months VRT phase (post 2) in each patient. The "short-term" variability (i.e. differences amongst the 6 HRP visual field examinations) as well as the "long-term" changes (i.e. the differences between baseline and post training and follow up examinations, respectively) are demonstrated. Patient B and patient D showed the greatest "short-term" as well as "long-term" visual field changes. The smallest "short-term" as well as "long-term" visual field changes showed patient E. Patient A and patient C showed a moderate extent both of "short-term" and "long term" visual field changes.

of the individual course of training based visual field changes in all patients. First, group results are presented, followed by an illustration of single case results (Fig. 1). Secondly, the "short-term" visual field changes amongst the six HRP measurements are shown for each patient at baseline, after the first 3-months VRT period, after subsequent 3-months follow-up without training and after the additional 3-months VRT phase (Fig. 2). Figure 2 also shows the extent of visual field changes after training ("long-term" changes). Finally, patients' perception of visual impairment before VRT and the subjective effects of VRT are described.

### *4.1. VRT-phase 1*

The effects of the first 3-months VRT period were as follows: four out of five patients had increased ability to detect visual stimuli in HRP. The group average improved by 12.45% ($Z = -2.023$, $p = 0.043$). In 30° W/W perimetry all patients displayed a stimulus detection improvement, which was on average 9.15% ($Z = -2.023$, $p = 0.043$). In the 70° W/W perimetry, which included more peripheral, non-trained areas, detection rate increased by 8.46%, but this was not significant. In B/Y perimetry there was only a small and insignificant improvement by 2.14% (Table 2).

Fixation performance increased both in HRP (5.6%), in 30° W/W (2.6%) and in 70° W/W perimetry (8.8%). In contrast, fixation rate slightly decreased in 30° B/Y perimetry ($-1.8\%$). None of these changes were significant (Table 2). No significant correlations were found between detection improvements in HRP or 30° W/W perimetry and fixation performance.

False hits were unchanged in HRP ($+0.68\%$) and increased slightly, but not significantly, in 30° W/W perimetry (8.4%) and in 30° B/Y perimetry (4.2%). In the 70° perimetric visual field test the average number of false hits decreased by $-3.4\%$ (n.s.) (Table 2). The number of false hits was not significantly correlated with stimulus detection in any of the visual field tests.

Visual acuity as well as contrast sensitivity increased in three patients after VRT and did not change in two

Table 2
Comparison of training visual function (visual acuity and contrast sensitivity) and visual field test results (stimulus detection rate, fixation rate and false hits) in HRP, 30° W/W, 30° B/Y and 70° W/W perimetry of baseline and post 1 assessment

| | Baseline | Post 1 | Percent change | Z (p) |
|---|---|---|---|---|
| Hits in HRP | 48.95 ± 16.9 | 61.40 ± 19.70 | 12.45 | −2.02* (0.04) |
| Hits in 30° W/W | 75.00 ± 18.66 | 84.15 ± 17.58 | 9.15 | −2.02* (0.04) |
| Hits in 30° B/Y | 85.10 ± 17.28 | 87.24 ± 18.68 | 2.14 | −1.21 (0.22) |
| Hits in 70° W/W | 60.62 ± 23.71 | 69.08 ± 17.75 | 8.46 | −0.40 (0.68) |
| HRP fixation | 93.10 ± 4.40 | 98.70 ± 0.64 | 5.6 | −1.75 (0.00) |
| 30° W/W fixation | 90.80 ± 14.68 | 93.40 ± 10.8 | 2.6 | −0.36 (0.71) |
| 30° B/Y fixation | 98.20 ± 4.02 | 96.40 ± 5.36 | −1.8 | −1.34 (0.18) |
| 70° W/W fixation | 83.00 ± 16.64 | 91.80 ± 13.46 | 8.8 | −0.81 (0.41) |
| HRP false hits | 3.37 ± 2.15 | 4.05 ± 3.00 | 0.68 | −0.67 (0.50) |
| 30° W/W false hits | 100.0 ± 0.00 | 91.60 ± 13.14 | −8.4 | −1.34 (0.18) |
| 30° B/Y false hits | 100.0 ± 0.00 | 95.80 ± 5.76 | −4.2 | −1.34 (0.18) |
| 70° W/W false hits | 96.60 ± 7.60 | 100.0 ± 0.00 | 3.4 | −1.00 (0.31) |
| Visual acuity sc | 0.375 ± 0.30 | 0.41 ± 0.35 | 0.035 | −0.73 (0.46) |
| Contrast sensitivity sc | 17.70 ± 14.22 | 20.36 ± 13.2 | 2.66 | −0.40 (0.68) |

Note: $n = 5$, * $p < 0.05$, study results as mean (%) ± SD, visual acuity as decimal fraction, response control is 100% when patients show no false hits.

Table 3
Comparison of training visual function (visual acuity and contrast sensitivity) and visual field test results (stimulus detection rate, fixation rate and false hits) in HRP, 30° W/W , 30° B/Y and 70° W/W perimetry of post 1 and post 2 assessment

| | Post 1 | Post 2 | Percent change | Z (p) |
|---|---|---|---|---|
| Hits in HRP | 68.57 ± 13.22 | 75.33 ± 13.89 | 6.76 | −1.82 (0.06) |
| Hits in 30° W/W | 91.62 ± 6.34 | 92.17 ± 6.18 | 0.55 | −0.36 (0.71) |
| Hits in 30° B/Y | 95.47 ± 3.51 | 94.16 ± 5.64 | −1.31 | −0.55 (0.58) |
| Hits in 70° W/W | 74.22 ± 15.58 | 76.03 ± 11.82 | 1.81 | −0.73 (0.46) |
| HRP fixation | 98.67 ± 0.75 | 97.91 ± 2.03 | −0.76 | − 0.73 (0.46) |
| 30° W/W fixation | 91.75 ± 11.78 | 97.25 ± 5.5 | 5.50 | −1.34 (0.18) |
| 30° B/Y fixation | 98.50 ± 3.00 | 98.50 ± 3.00 | 0.00 | 0.00 (1.00) |
| 70° W/W fixation | 89.75 ± 14.61 | 98.00 ± 4.00 | 8.25 | −1.06 (0.28) |
| HRP false hits | 3.78 ± 3.40 | 3.61 ± 2.71 | −0.17 | −0.73 (0.46) |
| 30° W/W false hits | 89.50 ± 14.17 | 88.00 ± 10.70 | −1.50 | −0.27 (0.78) |
| 30° B/Y false hits | 94.75 ± 6.07 | 97.50 ± 5.00 | 2.75 | −0.81 (0.41) |
| 70° W/W false hits | 100.0 ± 0.00 | 97.00 ± 6.00 | −3.00 | −1.00 (0.31) |
| Visual acuity sc | 0.42 ± 0.40 | 0.372 ± 0.32 | −0.048 | −1.34 (0.18) |
| Contrast sensitivity sc | 20.05 ± 15.21 | 15.85 ± 7.80 | −4.2 | −0.73 (0.46) |

Note: $n = 4$, * $p < 0.05$, study results as mean (%) ± SD, visual acuity as decimal fraction, response control is 100% when patients show no false hits.

patients. The group results did not reach significance for either measure (Table 2).

### *4.2. VRT-phase 2*

HRP measurements after the second VRT phase showed additional improvement of stimulus detection performance in three out of four patients which, on average, constitutes an additional improvement of +6.76% which, however, did not reach significance. In contrast, when the results of perimetric testing were analyzed, there were only slight changes in the number of detected stimuli after the second 3-months training (Table 3).

Fixation performance increased in the 30° W/W by an additional +5.5% and in 70° W/W perimetry by 8.25%. Performance remained basically unchanged in B/Y and HRP perimetry. Regarding the number of false hits, there was only a slightly but insignificant change in all visual field tests (Table 3). Neither the fixation performance nor the number of false hits correlated with any of the other outcome measures such as stimulus detection improvements.

Average visual acuity and contrast sensitivity decreased when compared with phase 1 – outcome (Ta-

Table 4
Comparison of training visual function (visual acuity and contrast sensitivity) and visual field test results (stimulus detection rate, fixation rate and false hits) in HRP, 30° W/W, 30° B/Y and 70° W/W perimetry of post 1 and follow up assessment

| | Post 1 | FU | Percent change | Z (p) |
|---|---|---|---|---|
| Hits in HRP | 61.39 ± 19.70 | 60.10 ± 17.85 | −1.29 | −0.94 (0.34) |
| Hits in 30° W/W | 84.15 ± 17.58 | 82.66 ± 21.16 | −1.49 | −0.36 (0.71) |
| Hits in 30° B/Y | 87.24 ± 18.68 | 85.86 ± 18.41 | −1.38 | −1.51 (0.13) |
| Hits in 70° W/W | 69.08 ± 17.75 | 67.63 ± 16.60 | −1.45 | −1.28 (0.19) |
| HRP fixation | 98.70 ± 0.64 | 97.32 ± 2.32 | −1.38 | −1.75 (0.08) |
| 30° W/W fixation | 93.40 ± 10.8 | 91.00 ± 9.27 | −2.40 | −0.36 (0.71) |
| 30° B/Y fixation | 96.40 ± 5.36 | 97.80 ± 3.19 | 1.40 | −0.53 (0.59) |
| 70° W/W fixation | 91.80 ± 13.46 | 97.00 ± 4.12 | 5.20 | −1.06 (0.28) |
| HRP false hits | 4.05 ± 3.00 | 3.01 ± 1.60 | −1.04 | −0.94 (0.34) |
| 30° W/W false hits | 91.60 ± 13.14 | 96.60 ± 7.60 | 5.00 | −1.34 (0.18) |
| 30° B/Y false hits | 95.80 ± 5.76 | 100.0 ± 0.00 | 4.20 | −1.34 (0.18) |
| 70° W/W false hits | 100.0 ± 0.00 | 97.20 ± 6.26 | −2.80 | −1.00 (0.31) |
| Visual acuity sc | 0.41 ± 0.35 | 0.37 ± 0.32 | −0.03 | −1.60 (0.10) |
| Contrast sensitivity sc | 20.36 ± 13.2 | 19.92 ± 10.29 | −0.44 | −0.40 (0.68) |

Note: $n = 5$, *$p < 0.05$, study results as mean (%) ± SD, visual acuity as decimal fraction, response control is 100% when patients show no false hits.

ble 3). Visual acuity after the second VRT period was basically comparable to data measured at baseline.

### 4.3. Stability of results after phase 1

After the first VRT period was completed, visual improvements remained stable after the non-training phase. In each of the visual field tests there was a small but non-significant decrease of detection performance (comparison post 1 – training vs. follow-up). This slight detection loss was similar among the different visual field tests (Table 4).

At follow-up we noted a small decrease of fixation performance both in HRP and 30° W/W perimetry. In contrast, perimetry fixation performance slightly improved in the B/Y and 70° W/W. The number of false hits did not change significantly in any of the visual field tests after the 3-months training free interval (Table 4). There were also no significant correlations of stimulus detection changes and any other quality control measure such as fixation performance or false hits.

Visual acuity and contrast sensitivity measures did not change significantly after the training free 3-month follow up (Table 4).

### 4.4. "Short-term" and "long-term" visual field changes

To display the variability of visual field test results, Fig. 2 shows for each patient the percent of detected stimuli in HRP over a series of six visual field tests performed at baseline, after 3-months of VRT (post 1), after 3-months follow up and after the additional 3-months of training (post 2). The extent of "short-term" visual field variability at baseline, i.e. changes of the number of detected stimuli among the 6 HRP examinations was as follows: more than 10% visual field range based test variability could be observed in patient B and patient D and less than 10% in the other three patients. The amount of „short term" visual field variability varied remarkably over the measurement periods (i.e. baseline, post 1, follow up and post 2) in patient B (range: 4.43%–13.5% variability) and patient D (range: 4.00%–20.05% variability) and remained quite constant in patient A (range: 4.85%–6.96% variability), patient C (range: 5.06%–7.38% variability) and patient E (range: 4.65%–4.85% variability). The "long-term" visual field changes, i.e. visual field differences between baseline and post training examinations, exceeded unequivocal the "short-term" variability in case of patient B and patient D. The magnitude of "short-term" and "long-term" visual field changes was approximately equal in patient A and patient C (Fig. 2).

### 4.5. Subjective effects of VRT

Three of five patients (patients A, C and D) did not report any subjective noticeable visual impairment in everyday life because they did not have subjective complaints at study entry. However, all of these patients became more aware of the location and size of the visual field defect after they underwent the baseline visual field examinations. They participated in the study due to their ambition to prevent further visual field deterioration. Despite lack of subjectively perceptible training effects all three patients were content with the treat-

ment. Two patients (patients B and E) reported feeling subjectively impaired by the visual field defect. Patient B described having difficulties climbing stairs and reading small letters in newspapers. In the post-treatment interview he stated that the training was helpful and that he could see more with both his right (trained) and left (non-trained) eye. Patient E reported being impaired by the visual field defect primarily at dusk and in dim light. Subjectively he did not experience any changes in his visual abilities after training.

## 5. Discussion

In standard perimetry as well as in HRP we found visual field enlargements which remained stable even after a 3-months training-free period in glaucoma patients. In HRP the mean stimulus detection rate increased further after an additional 3-months of visual stimulation. The greatest extent of visual field recovery took place during the first training phase in all patients, though it should be noted that two patients achieved remarkable additional recovery in the second training phase as well.

Detection performance did not improve after training in the B/Y perimetry. This result indicates that VRT induced visual field enlargements are specific to the stimulus and background color features. Similar results have been reported for a detection task employing SLO (Scanning Laser Ophthalmoscope) perimetry, which uses a monochromatic bright red background and dark stimuli (Reinhard et al., 2005). Alternatively, results could be explained by the reduced redundancy hypothesis (Glovinsky et al., 1993). The blue-yellow ganglion cells represent a sparsely populated group of all the retinal ganglion cells and they have minimal receptive field overlap. The reduced redundancy hypothesis states that because of this low density of receptive fields and small amount of redundancy functional losses can be discovered earlier in this pathway (Bayer & Erb, 2002; Johnson et al., 1993). We propose that this might be also the cause why it is difficult (or impossible) to achieve vision restoration with the method we employed.

The extent of visual field recovery was rather variable between patients. Two of five glaucoma patients showed remarkable stimulus detection performance gains, two patients achieved moderate improvements and one patient did not benefit from VRT. This is generally in agreement with reports in stroke and head injury patients, where about 1/3 of the patients are non-responders (Kasten et al., 1998; Mueller et al., 2003; Sabel et al., 2004). It is notable that larger training effects were observed in those patients who had a tunnel-view-like visual field defect with an intact central visual field and an area of residual vision located at the border between an intact and defective area (Fig. 1).

The two patients benefiting less from VRT were those with a transition zone located either between the absolute defective areas or around an absolute scotoma (Fig. 1). This is in agreement with our prior observations in stroke and trauma patients where the location and size of the area of residual vision was found to be a predictor of good recovery (Mueller et al., 2003). Thus, the principle that areas of relative defects ("residual vision") play an important role in the process of recovery of vision (Sabel & Kasten, 2000) is confirmed in glaucoma and it seems that the location of these areas is of crucial importance for the glaucomatous defects as well. Thus, restoration occurs primarily in patients with ARV's located near the intact/blind border. The level of training induced visual field improvement seems to be influenced also by the extent of the "short-term" visual field changes. The two patients whose average stimulus detection performance improved after VRT in the most pronounced way were also those that showed the greatest amount of spontaneous visual field fluctuations at baseline. This result does not suggest that the effects of VRT are an artefact of spontaneous "short-term" fluctuations because post-VRT visual field changes were above those fluctuations. However, it does imply that mechanisms involved in spontaneous fluctuations (possibly attention) may also be involved in VRT-induced changes (Poggel et al., 2004). In any event, further research is needed to determine specific prognostic features for successful training in larger samples of glaucoma patients.

One could argue that visual field improvements are explained by altered fixation behaviour. But fixation performance improved after VRT and remained unchanged both in HRP and in W/W standard perimetric visual field tests, respectively, i.e. in measurements which showed stimulus detection gains. Moreover, fixation performance did not significantly correlate with visual field enlargements. That eye movements can not explain the detection improvement after VRT has also been shown by recent studies monitoring fixation ability using an eye-tracker. In stroke and head injury patients eye movements are not altered in any notable manner by VRT (Kasten et al., 2006). However, to rule out eye movements as an alternatively explanation for detection improvements of glaucoma patients af-

ter VRT, eye tracking records should be integrated in future studies.

The follow-up diagnostic measurements after a training-free interval showed that the visual field size decreased only slightly and non-significantly after 3 months. After the training-free interval the level of stimulus detection performance was still above the pre-training test results in all visual field examinations. This result replicates earlier findings of stable VRT effects after training is discontinued (Kasten et al., 2001).

The results of this pilot trial suggest that visual field defects caused by retinal lesion respond to visual stimulation in a manner similar to those after brain lesions. However, one should be cautious to draw more general conclusions from the present study because the patient sample was very small and the study was designed as a pilot trial only. Without a placebo control group impacts of the Hawthorne effect can not be excluded, i.e. the glaucoma patients may have improved performance simply because of the attention they received from the experimenter. Yet, based on our studies a placebo-controlled, randomized, double-blind clinical trial is warranted to examine whether VRT represents indeed an effective intervention for visual field defects in glaucoma patients. In our small sample the majority of the patients were not able to perceive the visual field defect consciously. This indicates that these patients can normally compensate the visual filed loss very well, for example because they have just one affected eye. Otherwise, if both eyes are affected, many patients with glaucoma have to cope with serious problems in their every day life, and with increasing severity of visual field loss there is an increase in the number of self reported visual problems (e.g. Nelson et al., 1999). Such measures of daily life activities require additional study as well. The subjective outcome of visual training by glaucoma should be assessed by using standardized visual function questionnaires before and after treatment.

Additional mechanisms contributing to the visual field improvement seen after training are learning processes. A number of studies have shown that perceptual learning is involved in a variety of visual tasks which is often stimulus- and task-specific (Karni & Sagi, 1993; Poggio et al., 1992; Ramachandran & Braddick, 1973; Sowden et al., 2002). In the present study we have found no transfer of training to other visual tasks like B/Y visual field test, visual acuity test and functional acuity contrast test. However, a transfer of training effects to more peripheral, non-trained areas could be observed (detection performance in the 70 ° perimetry). In summery, our results suggest that glaucoma patients retain some visual system plasticity and that repetitive training leads to visual field improvement that is specific for task and stimulus attributes. Future studies will show if learning at early stages in the visual pathway plays a role in vision restoration.

The cellular mechanism of restoration in areas of residual vision located between absolute scotoma and intact areas of the visual field, e.g. relative scotomatous areas could possibly involve the network-like intraretinal connectivity. Retinal interneurons such as amakrine and horizontal cells participate in lateral processing of light perception in the physiology of converging and diverging down-stream information processing between the photoreceptors and ganglion cells (Janssen et al., 1996). VRT may affect these converging and diverging pathways and stimulate those cells which usually remain silent after loosing their direct connectivity partners. So far, VRT seems to stimulate parallel pathways and to activate those cells which are either partially damaged or undamaged but have lost their direct connection partners.

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