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Recovery of visual field defects: A large clinical observational study using vision restoration therapy

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Abstract. *Purpose:* In small experimental trials, vision restoration therapy (VRT), a home-based rehabilitation method, has shown to enlarge the visual field and improve reaction times in patients with lesion involving the CNS. We now evaluated the outcome of VRT in a large sample of clinical patients and studied factors contributing to subjective and objective measures of visual field alterations.
Methods: Clinical observational analysis of visual fields of 302 patients before and after being treated with computer-based vision restoration therapy for a period of 6 months at eight clinical centers in central Europe. The visual field defects were due to ischemia, hemorrhage, head trauma, tumor removal or anterior ischemic optic neuropathy. Primary outcome measure was a visual field assessment with super-threshold perimetry. Additionally, conventional near-threshold perimetry, eye movements and subjective reports of daily life activities were assessed in a subset of the patients.
Results: VRT improved patients' ability to detect super-threshold stimuli in the previously deficient area of the visual field by 17.2% and these detection gains were not significantly correlated with eye movements. Notable improvements were seen in 70.9% of the patients. Efficacy was independent of lesion age and etiology, but patients with larger areas of residual vision at baseline and patients $>$ 65 years old benefited most. Conventional perimetry validated visual field enlargements and patient testimonials confirmed the improvement in every day visual functions.
Conclusions: VRT improves visual functions in a large clinical sample of patients with visual field defects involving the CNS, confirming former experimental studies.

Keywords: Vision restoration, hemianopia, visual field deficits, plasticity, neurorehabilitation, visual training, brain damage

1. Introduction

Neurological rehabilitation of patients with brain damage is well established in motor rehabilitation, speech therapy and occupational therapy (Mark & Taub, 2004; Taub, Uswatte, & Elbert, 2002; Wolf et al., 2005) but standards for rehabilitation of visual impairments are still under discussion (Bouwmeester, Heutink, & Lucas, 2007; Pelak, Dubin, & Whitney, 2007). However, the former pessimistic view that the neural specificity and receptive field organization of the adult visual system cannot be modified has been gradually replaced by the concept that the visual systems possesses potential for neuroplasticity (Pascual-Leone, Amedi, Fregni, & Merabet, 2005; Ramachandran, Rogers-Ramachandran, & Stewart, 1992; Theoret, Merabet, & Pascual-Leone, 2004. For updated

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review on experience-dependent plasticity in the adult visual system see Karmarkar & Dan, 2006.). This is demonstrated by observing reorganization of receptive fields in cats and monkeys after damage (Eysel, Eyding, & Schweigart, 1998; Gilbert & Wiesel, 1992) and spontaneous recovery of vision in animals and patients (Pless & Lessell, 1996; Sautter & Sabel, 1993; Vanier, Miller, & Carson, 2000; Zhang, Kedar, Lynn, Newman, & Biousse, 2006). Regular training can improve visual functions as shown in experiments on perceptual learning in normal subjects as well as in amblyopic patients (Polat, Ma-Naim, Belkin, & Sagi, 2004). In recent years, visual plasticity in visual impaired patients has been induced by repetitive activation (training) of surviving neurons in partially damaged brain regions (Balliet, Blood, & Bach-y-Rita, 1985; Huxlin & Pasternak, 2004; Julkunen, Tenovuo, Jaaskelainen, & Hamalainen, 2003; Kasten, Mueller-Oehring, & Sabel, 2001; Kasten & Sabel, 1995; Kasten, Wüst, Behrens-Baumann, & Sabel, 1998; Mueller, Poggel, Kenkel, Kasten, & Sabel, 2003; Polat et al., 2004; Polat & Sagi, 1994; Sabel, Kenkel, & Kasten, 2004; Schmielau, 1989). This expands the residual visual field, resulting in some restoration of lost vision. In several small-sample clinical trials, a computer-based training program, vision restoration therapy (VRT), has been shown to significantly improve visual fields as documented in sub- und super-threshold perimetric measures. In an early pilot study (Kasten & Sabel, 1995) and a subsequent randomized, double-blind trial with 38 patients (Kasten et al., 1998), the border of the visual field shifted by 4.9°–5.8°. Enlargements (Huxlin & Pasternak, 2004; Julkunen et al., 2003) and improved reaction times (Mueller et al., 2003; Sabel et al., 2004) have been reported in other studies, although improvements did not transfer when more complex diagnostic visual field measures were used (Balliet et al., 1985; Reinhard et al., 2005). Improved detection performance remained stable for at least 23 months after VRT in an experimental sample (Kasten et al., 2001) and for an average of 3.8 years in a clinical trial with 24 patients (Gall, Mueller, Kaufmann & Sabel, 2006).

The aim of this study was to examine the efficacy of VRT in clinical practice by analyzing a large data pool of $>$ 300 patients in Europe. In this context the influences of demographic factors and disease factors such as etiology, type of visual field defect as well as the role of eye movements on outcome of VRT was determined. In addition, to examine whether subjective vision had improved standardized post-training semi-structured interviews were obtained. For the first time, a small sample of patients with anterior ischemic optic neuropathy (AION), which accounts for 90% of cases of optic nerve damage. (Rucker, Biousse, & Newmann, 2004), was also studied.

2. Methods

2.1. Patient base and inclusion/exclusion criteria

General exclusion criteria for VRT were photosensitivity, uncontrolled epilepsy, cognitive impairments interfering with training (learning, memory or attention deficits), history of uncontrolled psychosis, and total blindness. Data from all patients with pre and post-training diagnostic results, who were treated with VRT between 1998 and 2004 at eight clinical centers in Germany, Austria and Switzerland were considered for inclusion of the study. Of 331 patients, 302 (91.2%) met the following inclusion criteria as determined prior to the analysis: (i) eccentricity of visual field defect $<$ 56°, (ii) cerebral or pre-chiasmatic lesion, (iii) presence of residual vision, (iv) cognitively able to perform the task, (v) sufficient fixation ability, and (vi) at least two valid baseline and two valid post-therapy high resolution perimetry (HRP) test results. All AION patients had insisted on carrying out VRT despite explicitly being informed that VRT effects had not been studied in AION. In 29 patients testing parameters at baseline and final testing were not identical and therefore were consequently excluded from the study.

2.2. Demographic data

The study group consisted of 116 females and 186 males with an age of 52.11 $\pm$ 15.88 years (mean $\pm$ SD; range: 9.6–82.9 yrs). Average lesion age at onset of training was 2.66 $\pm$ 3.77 years (mean $\pm$ SD; range: 0.1–25.6 yrs) (Table 1), 5.7% trained within the first three months and 20.8% within the first six months after onset of visual field symptoms. Visual field defects, as documented by medical records, were caused by either lesions involving the post-chiasmal visual sensory pathway or pre-chiasmal lesions unassociated with any intraocular damage.

Table 1
Demographic data of study sample; age of patients, age of lesion (mean ± S.D.) and sex by etiology. *Six patients with bi-temporal field defects were counted once only in the analysis of demographic data but twice for analysis of visual performance, as each eye was considered to be independent

Cause of lesion	No. of patients	Sex		Age of patients (mean ± S.D.)	Age of lesion (mean ± S.D.)
		male	female		
Stroke	214	139	75	56.00 ± 13.33	2.20 ± 3.08
Trauma	43	25	18	35.60 ± 12.78	3.80 ± 4.03
Tumor	34	16	18	48.20 ± 18.06	4.10 ± 6.17
AION	5	3	2	67.10 ± 9.98	1.40 ± 1.88
Overall	302*	186*	116*	52.11 ± 15.88	2.66 ± 3.77

2.3. Protocol

All patients underwent two to five baseline assessments with super-threshold HRP before being entered in the study to validate the stability of visual field defect. After baseline assessment, VRT was carried out one hour daily, six days a week for six months at home, at the end of which outcome was measured again with repeated HRP ("final testing"). Training data was stored on a disk and controlled by the therapist. Between 1998–2001, standard perimetry and subjective improvement as part of standard clinic protocol was obtained in the Magdeburg clinic. Therefore, results of conventional perimetry and subjective improvements were additionally analyzed in the cohort who performed VRT during that period ($n = 69$). Additionally, in patients trained at the Department of Neurology, Bergmannstrost Halle/Saale eyetracker recordings were obtained ($n = 20$).

2.4. Diagnostic procedure

Visual fields were assessed with HRP in Magdeburg ($n = 208$) or at one of 7 other clinical centers ($n = 94$). Stimulus detection and average response time (ms) were measured as previously described (Kasten, Strasburger, & Sabel, 1997). Correct responses inside a tolerance time window (150–1000 ms) are termed "hits"; outside this window they are called false positives responses. Recording the patients' ability to detect near-threshold color changes of the fixation spot assessed adequate fixation (Kasten et al., 2001; Kasten & Sabel, 1995; Kasten et al., 1998). Hits were used to generate visual field maps in which blind regions are displayed in black and areas of residual vision (ARVs) in which performance was intermediate (Kasten & Sabel, 1995; Kasten et al., 1997) are displayed in various shades of gray (Fig. 1). The number of hits in HRP is a valid primary end point as it correlates closely with the number of misses (i.e. stimulus presentations to which the patients did not respond) in standard, near-threshold perimetry ($r = 0.79$, $p < 0.05$). HRP-parameter standard settings were: (i) fixation point: size 0.76°, luminance 100 cd/m^2, (ii) target stimuli: size 1.52°, color: bright gray (86 c/m^2), presentation time 150 ms; (iii) background illumination: 23 cd/m^2. HRP parameters may have varied depending of patients' visual abilities or by centers but were consistent at baseline and at final testing in every patient.

Monocular visual field changes were assessed with 90° conventional near-threshold perimetry (Rodenstock Perimat 206). This perimetric measures uses a staircase method with increasing luminance for stimulus positions where stimuli are not detected. Visual stimuli were green (560 nm) and were presented for a duration of 200 ms. The luminance increased (6 dB) in three steps until the dimmest target at each of the test locations was detected (luminance range 0.1–250 cd/m^2). Background luminance was 1 cd/m^2. The distances between stimuli increased by eccentricities and was set on average at 3°, 4° and 6° between 0°–10°, 10°–20°, 20°–30° respectively.

2.5. Fixation ability

In near-threshold perimetry, fixation was examined with a detection task at the fixation spot that the patients had to respond to by pressing a button. Additionally, fixation was monitored via video camera. The distance of the blind spot from the 0°-vertical meridian on the conventional, monocular perimetry charts were measured before and after VRT. HRP- examination was accompanied by a measurement of the patients' eye movements using an infrared eye-tracking system in 20 patients.

2.6. Vision restoration therapy

VRT (NovaVision AG, Magdeburg, Germany) is a home-based rehabilitation program that generates vi-

sual stimuli primarily in ARVs (Kasten & Sabel, 1995; Kasten et al., 1997; Kasten et al., 1998). All patients trained for six months (1 hour daily/six days a week). All sessions were stored on a disk and training parameters were adjusted monthly in response to changes in the visual fields after completion of a training month. VRT was used either binocularly ($n = 258$) or monocularly ($n = 44$) depending on whether heteronymous visual field deficits, strabismus or differences in visual acuity were present. 14 of the 44 patients training monocularly, practised with both eyes (in separate sessions). In these patients results of both eyes were averaged.

2.7. Subjective vision

Reports were collected in semi-structured interviews after training. Patients were asked to specify any changes in their visually guided daily activities. Five categories of improvement were considered: (i) general vision, (ii) confidence in mobility, (iii) reading, (iv) collisions with objects or people, and (v) hobbies.

2.8. Statistical analysis

Pre-/post-VRT differences were calculated with t-tests for paired samples (2-sided); within-group differences in HRP were tested with the Wilcoxon test. Differences between groups (e.g. type of lesion and type of visual field defect) were calculated post hoc by one-way ANOVA, with the gains in hits post-VRT as the dependent factor and the group as independent factor (post-hoc Bonferroni test). Age-related differences between groups were calculated using the Mann – Whitney U Test. The parametric Pearson's coefficient was used for correlation analyses except when the data had no normal distribution, in which case the non-parametric Spearman's Rho was employed (all data shown as mean $\pm$ SE unless otherwise specified).

3. Results

3.1. Primary outcome measures

After 6 months of VRT, the percentage of hits in HRP improved by an average of 9.7 $\pm$ 0.60% from 56.57 $\pm$ 0.85% at baseline to 66.30 $\pm$ 0.91% at final testing ($t = -16.13$, $p < 0.001$) (Fig. 1). This corresponds to a relative improvement of 17.2%. The detection rate varied considerably among patients. Applying the categories of improvements in detection measured by HRP established in an earlier clinical trial (Kasten et al., 1998), substantial improvements (10%–59% detection gains) were seen in 38.3% of patients; 32.6% showed moderate improvements (3%–10%); and 29.1% showed no improvements (-31%–3%). The change in the number of undetected stimuli in the intact part of the visual field was small (3.07 $\pm$ 0.34 at baseline, 1.94 $\pm$ 0.30 after VRT) whereas the number of undetected stimuli in the defective part decreased from 77.07 $\pm$ 1.42 to 61.98 $\pm$ 1.72 ($n = 238$). The gains were predominantly located in the former ARVs. These detection improvements resulted primarily from shifts in the visual field border, with field expansions averaging 4.9 $\pm$ 0.41°. The effect size for the improvements in HRP was estimated (Bortz & Döring, 1995) to be in the medium range ($d = 0.62$; > 0.5). In addition, the reaction time improved from 463.6 ms $\pm$ 5.08 ms to 446.2 ms $\pm$ 5.23 ms, i.e. by an average of 17 ms (range: -240 to $+223$ ms) ($t = 4.845$, $p < 0.001$) (see Fig. 1). The number of false hits increased significantly from 1.71% at baseline to 3.18% at final testing ($t = -6.647$, $p < 0.001$). In the 69 patients examined with conventional perimetry, the number of misses in the right eye decreased from 44.64 $\pm$ 2.41% pre-VRT to 37.14 $\pm$ 2.26% post-VRT ($t = 5.68$, $p < 0.001$), in the left eye from 49.79 $\pm$ 2.66% to 41.59 $\pm$ 2.58% ($t = -6.93$, $p < 0.001$). Correlation between improvement in HRP (in %) and conventional perimetry (result of both eyes averaged in %) was significant ($r = 0.437$, $p < 0.001$).

3.2. Detection gains related to demographic factors

Efficacy of VRT was independent of sex and did not correlate with either the age of the lesion or age of the patients (Table 1). However, when age was analyzed as a dichotomous variable, patients > 65 years (average age of retirement in Europe; $n = 71$) unexpectedly showed greater improvement (12.25 $\pm$ 1.54%) than patients < 65 years ($n = 237$; 8.93 $\pm$ 0.625%; $Z = -2.52$, $p < 0.012$).

Sub-stratification by etiology (Table 2) revealed that the cause of the lesion did not influence outcome (ANOVA, n.s.). All subgroups showed significant detection improvement, only the results of the AION-group (increasing by 7%), did not reach significance ($Z = -0.94$, $p = 0.345$). Type of visual field defect significantly influenced efficacy: patients with a diffuse topography of visual field defects benefited most (ANOVA, $F = 4.764$, $p < 0.001$) but patients with hemianopia or quadrantanopia also showed significant detection improvement after VRT (Table 3).

Table 2
Number of hits at baseline and final testing in HRP (mean ± S.E.) by etiology. *Six patients with bi-temporal field defects were counted once only in the analysis of demographic data but twice for analysis of visual performance, as each eye was considered to be independent

Cause of lesion	No. of patients	Number of stimuli in percent (mean ± S.E.)		Diff. (%)	Z-score	p-level
		Baseline	Final			
Stroke	214	58.12 ± 0.91	67.16 ± 1.01	9.04	−11.7	< 0.001
Trauma	43	55.87 ± 2.63	66.18 ± 2.83	10.31	−4.74	< 0.001
Tumor	34	48.75 ± 2.65	62.38 ± 2.66	13.63	−4.93	< 0.001
AION	5	53.01 ± 9.62	61.45 ± 12.16	8.44	−0.94	0.345
Overall	302*	56.57 ± 0.85	66.30 ± 0.91	9.73	−16.13	< 0.001

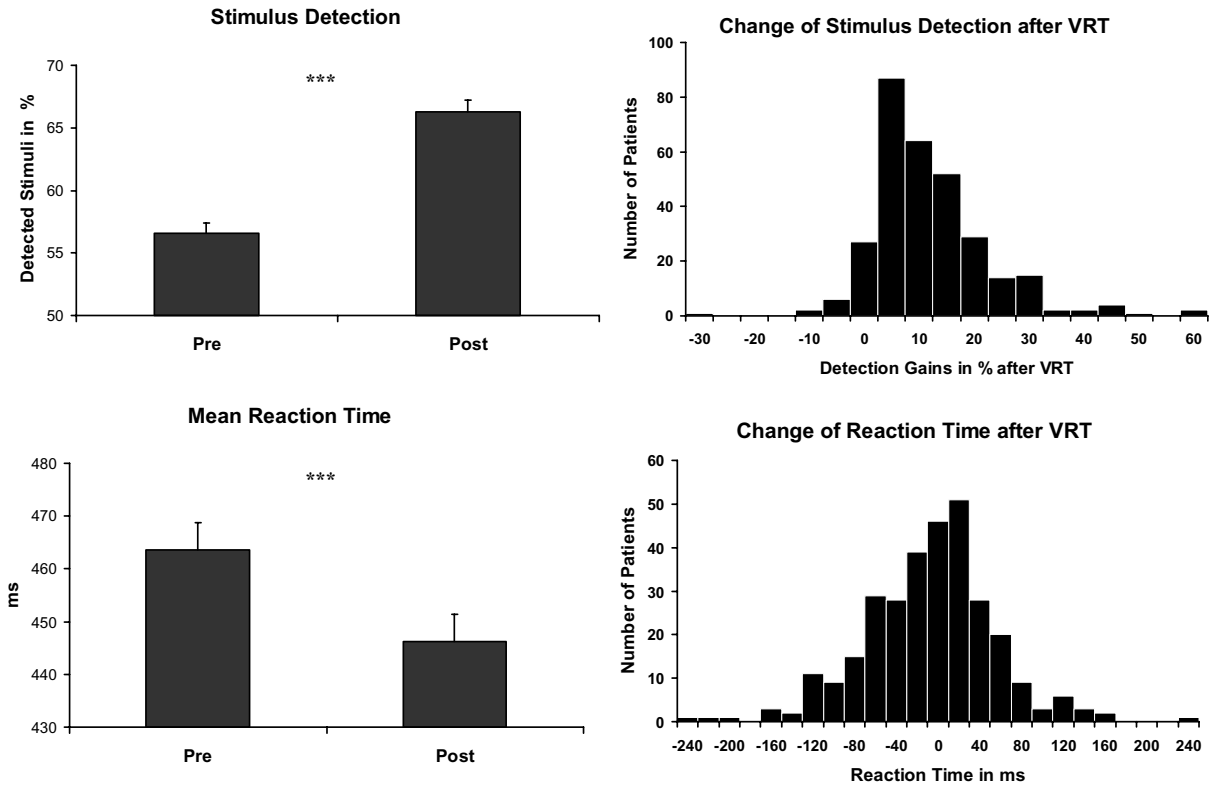

Fig. 1. Detection and reaction time charts in HRP. Average detection performance (upper panels) and reaction time charts (lower panels) for all patients, determined by HRP. Left: average performance of the total patient sample before and after VRT (mean ± SE). Detection is expressed as a percentage of maximum possible performance. Upper right: histogram showing the number of patients in each category of detection gains in steps of 2% (absolute changes). Lower right: reaction time histogram plotted in steps of 10 ms. Negative values display a decrease in reaction time, e.g. faster response time to stimuli after VRT.

3.3. Fixation ability and eye movements

The position of the blind spot as determined in conventional perimetry did not change post-VRT: pre/post values for the right eye were 13.44 ± 0.57°/13.44 ± 0.57°; for the left eye, 13.6 ± 0.97°/13.1 ± 1.67° (n.s.). Standard deviations of horizontal eye movements towards both sides increased significantly after VRT ($p < 0.001$) but this did not correlate with stimulus detection gains ($r = 0.038$, n.s.).

3.4. Correlation analyses

Gains detected by HRP after VRT (% improvement) showed significant negative correlation with fixation performance ($r = -0.239$, $p < 0.001$) and percentage of hits ($r = -0.260$, $p < 0.001$). Positive correlations

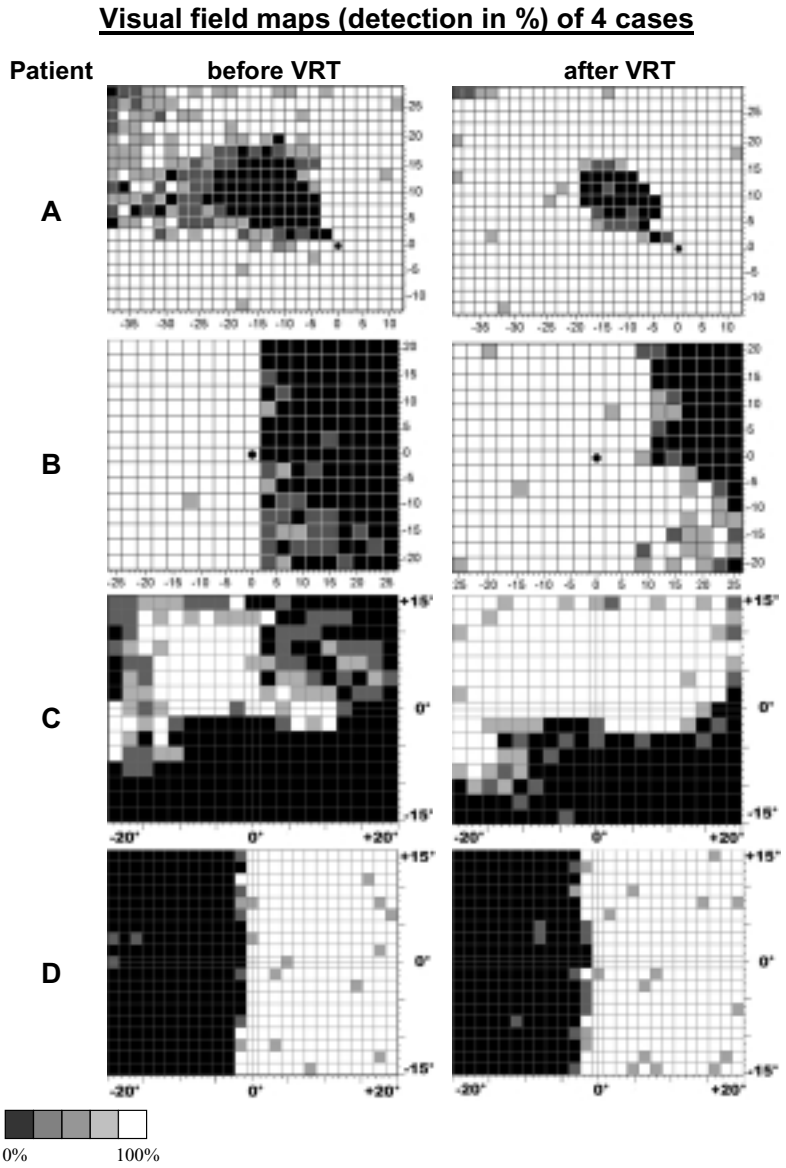

Fig. 2. Visual field charts of selected single cases. This graph shows representative visual field charts of four patients with lesions varying in size and location before (left) and after VRT (right). The first three patients show substantial improvement after VRT whereas the fourth is a typical non-responder. "Blind" regions are displayed in black; areas of residual vision (ARVs), where performance was intermediate, in various shades of gray; and intact visual fields in white. **Patient A,** a 56.2 year-old male, started VRT 6 months after ischemia in the region of the right posterior cerebral artery resulted in upper left quadrantanopia. His detection performance improved from 77% to 93%, fixation improved from 98.70% to 100% and false hits decreased from 27 to 20. **Patient B,** a 52 yr female, had a hemorrhage caused by an embolic aneurysm of the left posterior cerebral artery 11 months before starting VRT. She had a "complete" right hemianopia with a relatively large ARV in the lower quadrant. After VRT, detection increased from 56% to 79%, fixation increased slightly (from 95.60 to 98.60%) but false hits remained stable. Note that the border in the upper field shifted from about 2° to about 12° and in the lower quadrant only small deficiencies remained after VRT. **Patient C,** a 56.1 yr female suffering from optic nerve atrophy following a car accident 6 months before starting VRT, had a rather diffuse visual field defect that was more pronounced in the lower field. After VRT, stimulus detection improved from 32.86% to 58.92 %; fixation control remained almost unchanged (pre: 95.6%; post: 97.7%); false hits declined from 10 to 6. **Patient D** is a 49.4 yr female with a complete homonymous hemianopia on the left who started VRT 13 months after an occlusion of the right posterior cerebral artery. Additionally, the optic nerve was atrophic. The visual field size changed little (pre: 52.74%; post: 54.22%); fixation decreased slightly from 98.17 to 95.96%; and false hits increased from 7 to 35.

Table 3
Analysis of hits in HRP by type of visual field defect (mean ± S.E.). Patients with complete hemianopia have more than 90% blind positions whereas patients with incomplete hemianopia have less than 90% blind positions in one half of the tested visual field (by superimposing at least three HRP charts)

Type of lesion	No. of patients	Number of stimuli in percent (mean ± S.E.)		Diff. (%)	Z-score	p-level
		Baseline	Final			
Complete hemianopia	95	53.00 ± 0.33	60.28 ± 0.85	7.28	−7.75	< 0.001
Incomplete hemianopia	102	60.24 ± 0.65	70.68 ± 1.13	10.44	−8.28	< 0.001
Quadrantanopia	43	72.02 ± 1.97	79.23 ± 2.14	7.21	−4.58	< 0.001
Scotoma	6	91.70 ± 3.35	96.62 ± 1.33	4.92	−1.83	0.070
Diffuse defect	48	44.13 ± 2.68	59.03 ± 2.85	14.90	−5.41	< 0.001
Tunnel vision	8	24.24 ± 7.09	39.77 ± 8.78	15.53	−1.68	0.090

were found with number of false hits ($r = 0.168$, $p < 0.003$) and mean response time ($r = 0.378$, $p < 0.001$) at baseline assessment. Thus, patients with lower fixation performance, lower detection rate and a tendency to make more false hits at baseline showed greater improvements. Detection gains measured after VRT correlated significantly with the increase in number of false hits ($r = 0.254$, $p < 0.001$) and improvements in mean reaction time ($r = -0.238$, $p < 0.001$) but not with changes in fixation performance ($r = 0.078$, n.s.). This indicates that false hits contribute in a minor way to the total number of gains.

3.5. Subjective vision

The responses of the patients to the semi-structured interviews revealed that visual confidence had improved in the majority patients (75.4%); reading improved in 43.5%, 31.9% had fewer collisions with people or objects, and 29% had returned to former hobbies. About 12% reported no subjective changes. Significant correlations between subjective improvement and visual field size changes in HRP were found in the categories "carrying out hobbies" ($r = 0.360$, $p < 0.01$), "general improvement of vision" ($r = 0.244$, $p < 0.01$) and a trend for "reading" ($r = 0.215$, $p < 0.1$), but not for the categories "collisions or mobility" Fig. 2 (Mueller et al., 2003).

4. Discussion

Effectiveness of computer-based rehabilitation of cerebral visual field defects has been controversial. Besides clinical relevance, methodological designs have been debated. Vision stimulation trainings have been presented as randomized controlled trails (RCT), including double-blind procedures (Kasten et al., 1998) but until now, no larger clinical population has been studied (Pelak et al., 2007).

The results from this large clinical sample confirm the findings of smaller controlled studies (Julkunen et al., 2003; Kasten & Sabel, 1995; Kasten et al., 1998; Mueller et al., 2003; Muller, Sabel, & Kasten, 2006; Poggel, Kasten, & Sabel, 2004; Sabel et al., 2004) in experimental settings that 6 months of VRT significantly improves visual functions in patients with cerebral caused visual field defects. VRT lead to an improvement in detection ability, which increased the size of the visual field in the majority of patients as shown by two different perimetric methods using sub- and suprathreshold stimuli. In this clinical study, besides detection improvements, faster reaction times (see also Mueller et al., 2003; Sabel et al., 2004) in HRP after training were observed. Reaction time changes, however, have to be interpreted carefully in general because they can occur from multiple factors (e.g. such as test learning or internal change of decision criteria) which can not be totally excluded. However, other groups have also found improved VEP patterns after visual training in single patients (Julkunen et al., 2003), therefore it may well be hypothesized that repetitive training influences the speed of visual information processing in patients with visual field deficits, but this has to be verified in further studies. In terms of demographic prediction factors, the outcome of VRT was not found to be influenced by patients' age, sex, the etiology or the age of the lesion (Kasten et al., 1998; Mueller et al., 2003; Muller et al., 2006), so the mechanism of visual restoration seems to be independent of these factors. The one interesting exception are the significantly better outcomes in patients older than 65 years, suggesting that plasticity effects based on training are not restricted by older age. Functions of overall cognitive abilities e.g. perceptual speed (Lindenberger & Baltes, 1997) as well as sensory functions in everyday life are declining by age and both factors are correlated (Lindenberger &

Baltes, 1994). It can be speculated that cognitive factors, which are sensitive to age-decline, such as visual attention and speed of decision making, are also trained in elderly patients by VRT and this could contribute to somewhat greater training effects.

In contrast to previous small sample studies significantly more false hits were observed after VRT (Kasten et al., 2001; Kasten & Sabel, 1995; Kasten et al., 1998; Mueller et al., 2003; Wüst, Kasten, & Sabel, 2002). False positive responses may be caused either by an increase of late responses (they could be correct hits, too slow to fall within the 1000 msec time window) or due to changes of decision criteria. Whatever the cause is, a correlation analysis reveals that false positive responses contribute about 7% to the variance of detection gain.

The only reliable factor influencing outcome is the size of the area of residual vision: patients with greater areas of residual vision have greater plasticity potential compared to patients with no residual vision. Diffuse visual field defects present also larger ARVs, in which the neurons surviving the injury may drive the remaining partial function, which can then benefit from VRT (Sabel, 1997). Repetitive visual training presumably activates these residual neurons (Wüst et al., 2002), so the larger the ARV, the better the prognosis. This may also be the reason why patients with optic nerve damage, who typically have large ARVs, show greater field enlargements following VRT (Kasten et al., 1998).

The effects of VRT on patients with anterior ischemic optic neuropathy have been studied here for the first time. The five treated patients showed an average increase of 7% of visual detection in HRP. This value was primarily due to one patient showing improvements of 40.14% respectively, three minor changes of 3–5% or no changes (−9%). Though it is too early to determine whether AION patients profit from VRT, they have, just like patients with brain damage, also areas of residual vision, which seem to be a requirement for vision restoration. In contrast to the situation after stroke or head injury, these areas of residual vision are caused by ischemic lesions in the anterior part of the optic nerve. Significant improvements after systematic visual stimulation have been demonstrated in patients with pregeniculate lesions before (Kasten et al., 1998), suggesting that restoration of vision can be induced in patients with lesions in the more peripheral visual pathway and is not limited to post-chiasmatic lesions. Further efficacy studies are warranted to determine whether some vision can be restored in AION patients.

The majority of patients report ADL specific improvements after VRT, confirming previous observations (Kasten et al., 1998; Mueller et al., 2003). This correlated to a small degree with objective visual field enlargements. While even patients with small visual field enlargements noted subjective improvements due to VRT, surprisingly some of the patients with greater improvements did not state any changes in their daily life after VRT. It can be concluded that the relationship of subjective improvement after vision therapy to objective measures of vision is a rather complex one, probably involving other factors such as expectations before training, general awareness of cognitive and sensory deficits and topography of visual field defect and this should be further explored. Furthermore, subjective improvements are unlikely to result solely from spatial expansion of the visual field but also from changes in visual information processing speed, which may be also altered after systematic light detection training. Indications that training effects may be transferred into daily life activities may be also drawn from the fact that visual field size improvements correlate significantly with independent paper-pencil tests of speed visual search test and spatial attention (Kasten, Bunzenthal, Müller-Oehring, Mueller, & Sabel, 2007).

The question arises whether visual field enlargements may be a consequence of possible eye movements towards the blind field (Balliet et al., 1985; Reinhard et al., 2005; Sabel et al., 2004). The converging control measures of eye movements indicate that the gains in detection in perimetric measures after VRT do not result from eye movements or eccentric fixation behavior, confirming other studies using eyetracking recording during visual training (Kasten, Bunzenthal & Sabel, 2006).

How VRT improves residual vision in neurophysiological terms is still unclear, but receptive field reorganization similar to that seen in animals (Eysel et al., 1998; Gilbert & Wiesel, 1992) may increase the excitability of peri-lesion areas of damaged visual cortex and/or in regions partially deafferented by pregeniculate damage. Although the strengthening of such bottom-up activation has not been examined in humans, top-down attentional influences impinging on the partially deafferented regions have been demonstrated to facilitate vision restoration in hemianopic patients (Poggel et al., 2004). Most recently, studies using imaging methods (such as Henriksson, Raninen, Nasanen, Hyvarinen, & Vanni, 2006; Julkunen et al., 2006; Marshall, Ferrera, Barnes, Zhang, O'Brian, Chmayssani et al., 2007) provided initial insight into the mechanism and brain regions of reorganization of the impaired visual systems after intense training.

In summary, the study confirms for the first time in a large clinical sample objective training-induced visual function improvements in patients with visual field defects. Improvements of the visual fields can be demonstrated with both super-threshold and conventional, near-threshold perimetry. Retrospective analysis of the large sample also presents reliable evidence that the efficacy of VRT is not influenced by the age or sex of the patient, the etiology or age of the underlying lesion. In addition, the increase in detection performance is accompanied by improvements in some daily life activities as assessed in semi-structured interviews. Therefore, systematic computer-based visual field training, especially of patients with large ARVs at baseline, can be effective to restore some of the visual functions in brain damaged patients even after spontaneous recovery is completed.

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Potential conflict and interest disclosure

Iris Mueller has no conflict of interest. Henning Mast is a consultant of NovaVision Inc. Bernhard A. Sabel is shareholder of NovaVision Inc.

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