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Visual field enlargement after computer training in brain-damaged patients with homonymous deficits: an open pilot trial

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Abstract

Brain damage is often accompanied by homonymous hemianopia, but few therapeutic approaches exist for visual field deficits. In this open pilot study we describe a computerized training program which may possibly reduce the size of the 'blind' visual field in patients with homonymous visual field deficits. Various stimuli to test light perception and discrimination of colors and shapes were presented on a monitor which permitted the examination or training of the central section of the visual field up to about 25° vertical and 40° horizontal eccentricity. Eleven patients trained at home for 1 h each day for a total of 80–300 h. Their results were compared with those of three patients who opted not to participate in the training procedure or those with very little therapy. These latter subjects had a slight decrease in the visual field size after about 1 year. In contrast, the treatment group displayed a reliable enlargement of visual field size. This was revealed by a significant improvement in the detection of small light stimuli, an increase in the ability to discriminate colors and a minor, but notable, improvement of shape discrimination in the blind areas of the visual field. Additional training of shape recognition led to further improvement of shape discriminations, even when the patients trained with very different kinds of shapes, e.g. lines or letters. Outcome depended on age of the patients and the size of the lesion, but it was independent of on-set of treatment and cause of the lesion. Only two of the 11 patients with treatment showed no significant improvement. This study suggests that regular home training of the 'blind' visual field with computer-controlled stimuli may lead to improvement in vision. However, because of the following methodological limitations results are only preliminary: (1) the trial did not contain a true placebo group, (2) the patients were not assigned randomly to a control or treatment condition, (3) the lack of defined inclusion criteria considerably increased the variance in neuropsychological performance, (4) because the experimental design was not double blind, experimenter bias cannot be ruled out, and (5) the conditions of the home training could not be standardized. The results warrant a larger randomized, double-blind controlled trial.

Keywords: Hemianopia; Visual system; Rehabilitation; Brain damage; Recovery of function; Neuroplasticity; Neuropsychology

1. Introduction

A considerable number of patients now survive brain damage due to stroke of the posterior cerebral artery or head injury of the occipital lobe. About 20–30% of such patients suffer from deficits in vision with need of therapy [19]. While the resulting homonymous hemianopias or quadrantanopias can be quantified by standard diagnostic procedures, there are only few therapeutic approaches for the treatment of visual field deficits.

The attempts to improve function by training were initiated in the beginning of this century, when Poppelreuter [29] trained World War I veterans with brain damage to overcome reading disabilities. Also special mirror glasses were employed to project the unseen part of the visual field onto the intact area [3,5]. However, most patients were confused by the double pictures of the left and the right visual half in the same part of the retina. Likewise, others used fresnel prisms for this purpose with essentially similar conclusions [22,23,32].

A simple way to compensate for a hemianopic visual deficit is the training of compensatory eye movements toward the direction of the blind field as described by

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Zihl [43–47]. He developed an automated device for saccadic eye-movement training, the 'electronic reading and exploration apparatus' (EREX). A light spot was presented on a large TV-monitor at different positions, the distance from the fixation point and the size of the stimuli were adapted to the enlargement of the blind area, and the patient was asked to find the stimulus only with one saccadic movement of his eyes without turning the head.

The results of these and similar studies [4,19,24,25, 43–47] can be summarized as follows: all authors trained the patients for a total of 8–27 sessions of 30–45 min each. Even with this small number, they found significant improvement of the saccadic eye movements into the blind area. For example, Zihl [44] and Kerkhoff et al. [19,20] found an average of 20–30° enlargement of the area scanned by eye movements, thus compensating for the deficit. However, only one of these studies reported a significant reduction of size of the blind visual field; Kerkhoff et al. [20] found a training-related visual field increase in 12 of 22 patients (mean increase 6.7°). Thus, while compensatory eye movements might improve the subjects visual performance by using the intact sector of the visual field ('compensation'), this approach has only minor advantages for real enlargement of the visual field.

A treatment of visual deficits from cerebral injury has not been regarded as possible for many centuries. In contrast to this traditional view, new studies with both animals and humans indicate that restitution may indeed be possible. Pöppel et al. [26–28], for instance, pointed out that the visual system has some capacities for plasticity after damage. Likewise, in animal studies Sautter et al. [34] and Sautter and Sabel [35] have tested rats' ability to perform a visual task after optic nerve crush or after intraocular NMDA-injections [33]. After the initial 'blindness' there was a significant recovery to near-normal performance levels even though only about 11–15% of the retinal ganglion cells remained connected to their principle brain targets. These results point toward the capacity of surviving neuronal elements, i.e. the spared retinofugal fibers, to undergo dynamic changes which may be involved in functional restitution.

In patients with visual deficits, a reduction of the visual impairment by a training of the residual visual capabilities has also been seen. For example, Zihl [42] who trained patients with homonymous hemianopia, found a small expansion of visual field borders during repeated measurements of incremental thresholds at the same retinal location. Kerkhoff et al. [19,20] and Pommerenke and Markowitsch [25] noted a minor average enlargement of the visual field borders up to 1° to 6.7° of visual angle. In contrast, Balliett et al. [2] trained 12 patients after stroke in the occipital lobe with this method and were unable to find an enlargement of visual field borders. They argued that dynamic measurements with the standard Tübinger perimeter [described in 23] can produce apparent, but not real, visual field enlargements. The apparent visual field enlargements disappear in a follow-up examination with an automatic (static) perimeter. Schmielau [36] trained two patients for about 300 h on a standard Tübinger perimeter and found an enlargement of the visual field borders.

Based on this evidence we have designed a study to address the following questions:

(1) Is it possible to reduce the size of blind areas in patients with visual field deficits by long-term training of the visual field borders?
(2) Is it possible to distinguish the treatment effects from spontanous recovery?
(3) Is it necessary to carry out separate training for each visual function (light perception, shape recognition, color discrimination) or are there generalized effects from one modalality to another?
(4) How do variables such as time since lesion, age of the patient, size of the visual field deficit and cause of the lesion, influence outcome?

2. Material and methods

2.1. Diagnostic procedures

2.1.1. Perimetry. To determine the size of the blind areas of each eye we used a standard Tübinger perimeter and performed dynamic measurements in our laboratory. The stimulus size was 12′, the luminance 318 cd/m^2, with the surround luminance of 6.35 cd/m^2. A small red fixation point was presented at the center of the visual field. We investigated the whole visual field up to 90° eccentricity to obtain evidence of our training for the total visual field.

Balliett et al. [2] criticized dynamic measurement and stated that when using static perimetry, the enlargement fades. For this reason we not only applied dynamic measurements with the Tübinger perimeter but performed, in addition, static perimetry with various computer programs developed in our own laboratory. Our diagnostic programs, PERIMAT, PERIFORM and PERICOLOR (see Section 2.2), are a type of automated perimetry, where the stimuli were presented on a screen instead of a hemisphere. These programs allow for a more exact, static testing of visual functions than commercially available perimeters. Vision was assessed using tests for fixation ability, detection of light stimuli, discrimination of orientations or recognition of color. Here, the patient was asked to look at a fixation point during the entire examination. All programs investigated (or treated) the mid-section of the visual field up to 12.5° vertical and 20° horizontal eccentricity (fixation point at the center of the monitor) or up to 25° vertical and 40° horizontal eccentricity (fixation point posi-

tioned at one of the four borders or corners of the screen; Fig. 1). The visual field beyond 40° eccentricity was not examined or trained with the computer monitor.

All tests were done in a darkened room, the head of the subjects was stabilized with a head-support. The fixation ability was tested with the FIXTRAIN program (Section 2.3.5), a control of eye movements was done with a small telescope on the Tübinger perimeter during the examinations. Inadequate fixation was an exclusion criterion, the data of some other patients with unstable fixation were excluded from further analysis. The stimulus was presented randomly on the screen in the blind and intact areas of the visual field. There was no acoustic signal prior to the visual stimulus. Therefore, anticipatory eye movements toward the stimulus were not possible. The brightness of all stimuli was above visual threshold (luminance is described in Section 2.2). Each item was presented at a given screen position only once. The correlation between the first and the second measurement with the computer programs (before therapy) was $r = 0.94$, indicating that the retest reliability of our tests was excellent.

2.2. Diagnostic programs

2.2.1. PERIMAT. This program measured the responses to small light stimuli which were presented in random positions on a black monitor screen for 150 ms. The visual angle of the stimulus was 0.2°, 1.5–5 mm diameter and the luminance, measured with a mastersix apparatus, at a distance of 30 cm from the screen, was 0.34–0.36 cd/m^2. The fixation point could be set either in the center or in one of the four corners of the screen in order to increase the size of the testable visual field. While fixating, the patient was asked to press the spacebar, as soon as perceiving the small light stimulus. The stimulus was presented at 500 different positions (20 × 25 matrix), within a period of about 20 min. All diagnostic tests were easily performed by normal subjects. Healthy subjects ($n = 15$) achieved an average of 99.6% correctly perceived stimuli in this kind of test.

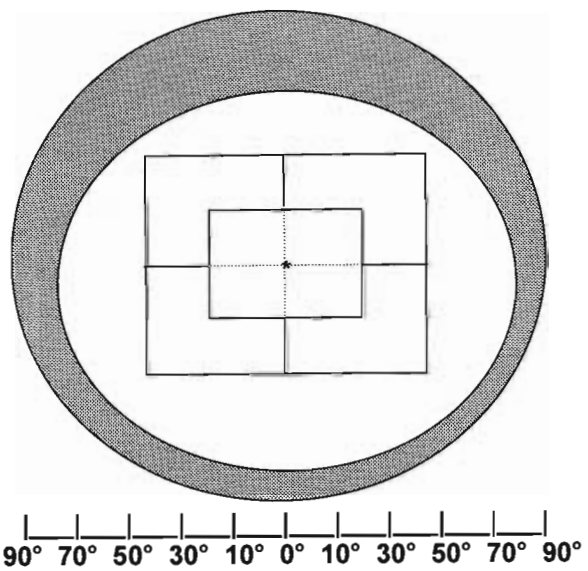

Fig. 1. Size of the visual field examined with a personal computer. The large outer circle shows the maximum extent of the human visual field (90°). The typical visual field is usually smaller, as shown here by the inner circle (60–80° eccentricity). The inner square shows the size of visual field that can be examined when the fixation point is positioned in the middle of the screen (40° latitude, 25° longitude). The large outer square shows the areas of the visual field that one can investigate when setting the fixation point in each corner of the screen (four examinations). The star indicates the position of the fixation point.

2.2.2. PERIFORM. The PERIFORM program examined the patient's ability to recognize orientations. The patient had to differentiate between four white lines (—, |, / and \). The visual angle of the lines was 0.93°, 7 mm long, and the luminance at a distance of 30 cm from the screen was 8.9–12 cd/m^2). The luminance differences were too small for a distinction of the lines without real orientation perception (tested with a milky-white glass before the screen in two normal subjects). The lines were presented randomly on black background for 150 ms. A session consisted of 260 presentations at different positions of such lines (20 × 13 matrix) in a period of about 15 min. Upon identifying the orientation of the line, the patient was asked to press one of four marked keys. Healthy subjects achieved an average of 95.6% correct choices in this test. In normal subjects there was a small learning effect in the PERIFORM and in the PERICOLOR programs. In repeated measurements of all four quadrants of the visual field we found an improvement of 3.4% due to better identification of the key caps.

2.2.3. PERICOLOR. This program assessed color perception. The patient was instructed to differentiate between four colored squares (green, red, blue and grey). The visual angle of the used square was 1.6°, while luminance at a distance of 30 cm from screen for all colors was 0.5 cd/m^2; at a distance of 0.5 cm from screen: green 2.9 cd/m^2, red 3.2 cd/m^2, grey 2.4 cd/m^2 and blue 4.4 cd/m^2. The luminance differences were too small for a distinction of the colors without real color perception (tested in three color blind patients). The squares were presented in a consecutive manner on black background for 150 ms. One session consisted of 260 presentations of colored squares on different positions (20 × 13 matrix). Upon identifying the color of the square, the patient was asked to press one of four marked keys. Healthy subjects achieved an average of 95.8% correct choices.

2.3. Therapy programs

In addition to the diagnostic programs, we developed therapy programs for Commodore 64 and MS-DOS personal computers. The patients received a disk with the software adapted to their respective deficit and they were instructed to train for 1 h each day in a darkened

room at home. The size of the TV-screen or monitor was measured and the distance between patient's eyes and the screen was adjusted that a training within 40° eccentricity was possible. The results of every session were saved on disk for subsequent analysis. As soon as the patient performed at a pre-determined level (>90% correctly recognized stimuli), the program advanced to a more sophisticated level, i.e. stimuli were presented further out in the blind visual field section. The therapy programs had two different sounds as a feedback to let the patient know whether the reaction was successful or not. The size of trained visual field was identical to that of the diagnostic programs. There was no control of fixation of the eyes, but the patients were instructed that the treatment would not be successful without a stable fixation. As proved by the high number of training sessions, we believe that all patients were highly motivated to do so.

2.3.1. VISURE. This program was developed to train the border between the intact and the deficient sectors. Here, a large white stimulus was moved from the healthy visual field into the borderline area. The patients were asked to press a key whenever they were able to perceive the symbol. The stimulus then moved further into the direction of the blind area and flickered in this position for 5–10 s. If the patient was unable to see the stimulus at this position, the stimulus retracted back into the intact area and the procedure was repeated.

2.3.2. SEETRAIN. In this program, the patient had to detect a stimulus on a black screen. The brightness of the stimulus changed from dark gray to light white in the same position. Another training method was based on the perception of a growing black line on a gray screen. The patients were asked to press the key as soon as they perceived the stimulus. Both parts of this program had the feature of adapting to the specific deficit of any patient by changing the appropriate stimulus parameters such as size or brightness.

2.3.3. FORMTRAIN. This is a discrimination training program for recognizing several geometrical figures such as squares, circles or triangles. Patients were asked to discriminate the line orientation or to distinguish between the letters A, B, C and D. FORMTRAIN allowed the choice of larger or smaller lines, letters or shapes for a stimulus presentation time between 150 and 500 ms. Since the latency of saccadic eye movements is about 175–200 milliseconds, we trained our patients with a stimulus presentation of 150 ms. Usually the stimuli were presented at different positions at or near the border between intact and damaged visual field.

2.3.4. COLORTRAIN. This program trained the capabilities of color perception in damaged visual areas. The program showed squares with different colors and different size (visual angle: 1.6°; same colors as in the PERICOLOR program). All the other parameters were the same as in the FORMTRAIN program.

2.3.5. FIXTRAIN. This fixation-training program included several procedures for patients with inadequate fixation. For example, in one part of the program ('Position-Change') a medium (visual angle of stimulus: 0.66°, movements: 0.8°) or small square (visual angle of stimulus: 0.4°, movements: 0.4°) was presented on the middle of the screen. After a random time, the square moved a few millimeters away from its old position and the patient had to press a key immediately. Patients with impaired fixation capabilities were usually not able to recognize such small movements. In our study, we used this program not only for a training but for diagnostic examinations of the fixation ability, i.e. to examine whether the patient was able to keep the fixation stable for a sufficient period of time; 5% mistakes were tolerated in one session of 5 min.

The outcome of the training was evaluated with the three computer programs PERIMAT, PERIFORM and PERICOLOR (Section 2.2). In addition, we performed one (or more) dynamic examinations with the standard Tübinger perimeter. In contrast to the borderlines of the visual field which can be obtained with the Tübinger perimeter, the static measurement obtained with the computer programs provided quantitative data of correctly detected stimuli, thus permitting a statistical analysis of the follow-up measurements when compared to baseline. For this reason, the following data are primarily based on the results of the computer-assisted diagnosis, although we also analyzed the Tübinger perimeter results. The outcome measure 'percent increase' is defined by the number of correct choices within the trained area of the visual field (up to 40° eccentricity) and does not relate to the entire visual field.

2.4. Method validation

The three diagnostic programs PERIMAT, PERIFORM and PERICOLOR were standardized with a group of 15 healthy young adults (students). In addition, we examined three brain-damaged patients without visual deficits to determine whether a reduced attention span had any influence on our results. We also used the data of the undamaged halves of the visual field of our hemianopic patients to validate the method (Table 1).

2.5. Patients

Fourteen patients (8 women, 6 men) with an average age of 48.5 years were studied. Ten of these patients suffered from a stroke of the posterior cerebral artery, two had tumor operations, one had a skull fracture from an accident and one had suffered from a hemorrhage. The operational definition of homonymous anopias were, (a) matching deficits in both eyes with respect to the vertical midline and (b) known structural damage of the postchiasmatic visual system as documented by, for example, CT, X-rays or reports of surgery. The deficit shown by perimetry of patients C and H exceed the ver-

Table 1
Percentage of correct responses to visual stimuli and average reaction time (ms) for the diagnostic programs PERIMAT, PERIFORM and PERICOLOR

Computer programs	Correct responses (%)			Reaction time (ms)		
	Group H	Group BD	Group VD	Group H	Group BD	Group VD
PERIMAT	99.7	98.0	97.8	360	350	690
PERIFORM	95.6	90.0	76.5	940	1150	1030
PERICOLOR	95.8	92.0	86.0	860	970	890

We investigated healthy subjects (group H, $n = 15$), brain-damaged patients without a visual deficit (group BD, $n = 3$) and the intact halves of the visual field in brain-damaged patients with visual deficits (group VD, $n = 14$). The VD group has deficits of visual attention in the healthy parts as indicated by a prolonged reaction time in the PERIMAT program.

tical midline. Patient H had an accident with damage of the occipital lobe and a fracture of the skulls base. Patient C suffered strokes of both posterior cerebral arteries and, therefore, both hemisheres had deficits.

Patient A refused to perform the training task after the pre-screening; patients B and C discontinued the training after only 2 and 65 h, respectively, but agreed to participate in the follow-up examinations. To allow for a comparison to the results of the treatment group, the data of these three patients were pooled to constitute a 'control' group with little or no therapy. Table 2 summarizes the patient characteristics and Fig. 2 displays the size of the respective visual field deficits. Fig. 3 shows the same data for the second group (little or no treatment). Both figures also indicate the quadrant which was trained. The average age of our treatment group was 42.5 years, whereas the average age of our three subjects in the second group was 70.6 years. In addition, the size of the blind area in these three patients was larger than in most subjects of the treatment group. For these reasons the value of this second group as a true control is rather limited.

2.6. Training procedure

Before commencing therapy, patients underwent a screening procedure. This included one examination of the fixation ability (FIXTRAIN program) and several examinations of the size of the visual field deficit with the standard Tübinger perimeter and the three diagnostic programs (PERIMAT, PERIFORM, PERICOLOR). Perimetry was carried out separately for the right and the left eye. When both eyes had a matching deficit, this was considered to be a homonymous visual field deficit. Training was then performed binocularly with both eyes. All computer-assisted diagnostic measurements were conducted with a 14″ computer monitor that was positioned at a distance of 30 cm from the patients eyes. In this manner, we were able to examine the central visual field up to 25°/40° vertical/horizontal eccentricity. The four quadrants (upper right, upper left, lower right and lower left) were tested separately. To determine the reliability of the measurements, the trained quadrants of the patients (Fig. 2) were investigated several times before commencing therapy. Following baseline assessment, patients received a

Table 2
Patient description: identification code, age, sex, cause of lesion, time since lesion (months), duration of computer training (h) and improvement due to training (%)

Patient code	Age	Sex	Cause of lesion	Time since lesion (months)	Training (h)	% Increase (PERIMAT)
A*	76	f	SPA	5	none	0
B*	80	m	SPA	2	2	4
C*	56	m	Bilateral SPA	0.5	65	9
D	38	m	Tumor	5	70	7
E	56	m	SPA	2	83	−19
F	29	f	Cerebral hemorrhage	12	91	38
G	66	f	SPA	24	110	15
H	21	f	Brain injury	240	130	46 (PERIFORM)
I	26	f	SPA	2	156	20
J	41	f	Tumor	8	182	34
K	38	f	SPA	2	195	71
L	51	f	SPA	1	216	43
M	57	m	SPA	120	229	31
N	45	m	SPA	2	300	54

*Patients with little or no therapy.
SPA, stroke of posterior cerebral artery.

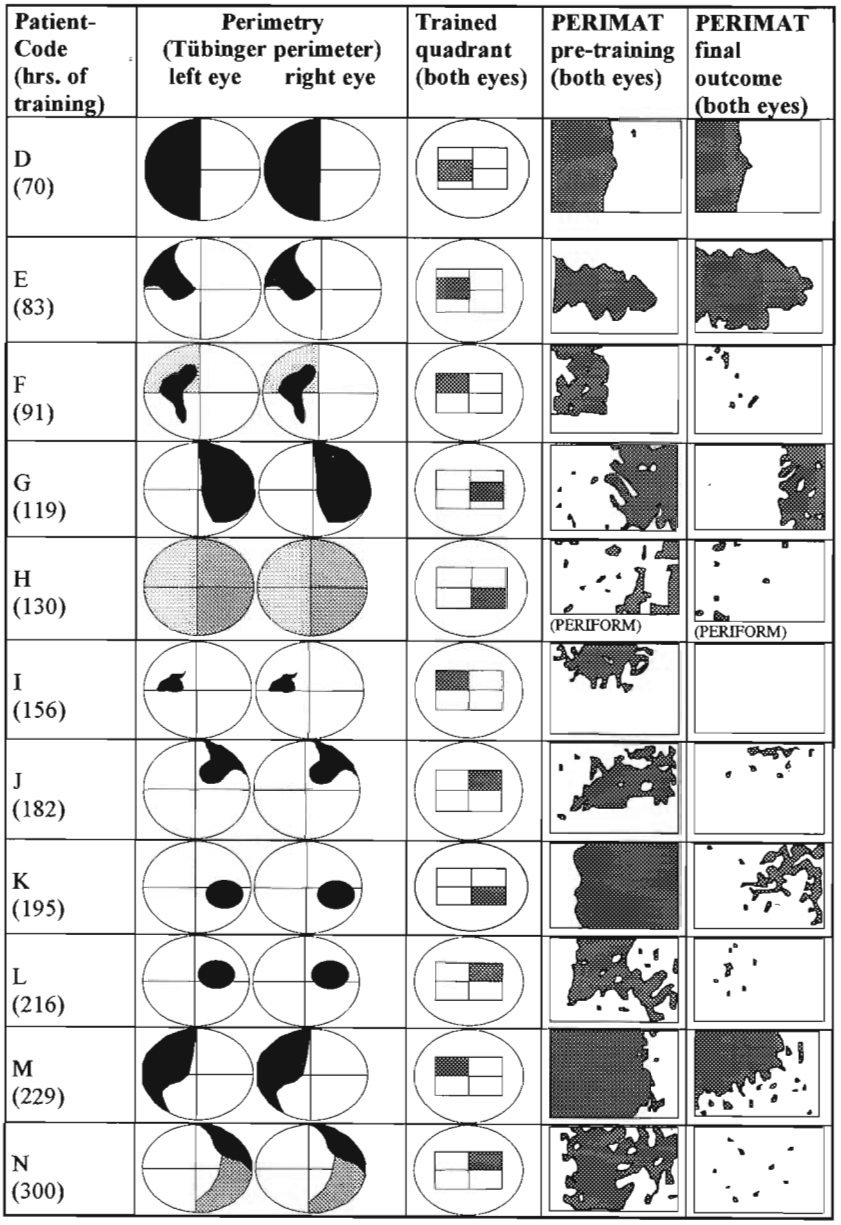

Fig. 2. Visual field size and training area. The graph shows, (A) the identification code of the patient, (B) the result of the perimetry; left and right eye were tested separately. Each circle represents the visual field of each eye up to 60° eccentricity, black indicates blind areas, shaded parts represent fields of inadequate vision, i.e. in repeated examinations of the same section the stimuli were sometime perceived and sometimes not, and white sections represent intact areas. (C) Display of the four possible monitor positions in relation to the visual field squares. The circle shows the binocular visual field, the small gray square is the area which was trained. (D) Is the result of the PERIMAT program in the training area before training commenced and (E) the same measure after training.

computer disk for their home training. This program was adjusted to the size of their specific visual field deficit. Generally, we chose the quadrant of the visual field for treatment which displayed the most severe deficit. Only when the patient suffered from a complete hemianopia, the mid-section was trained (Fig. 1). The patients were instructed to practice 1 h daily at home either on a TV-screen, which was connected to a Commodore 64 computer, or on a PC-controlled computer monitor in a darkened room. We assume that in the dark the stimuli would best enhance residual activity of the damaged visual system.

To approximate standardized training conditions, the distance of the patients to the screen was kept constant. Of course, with home-training, standardized conditions cannot be guaranteed. Thus, poor or good progress could depend, at least in part, on different training conditions at home.

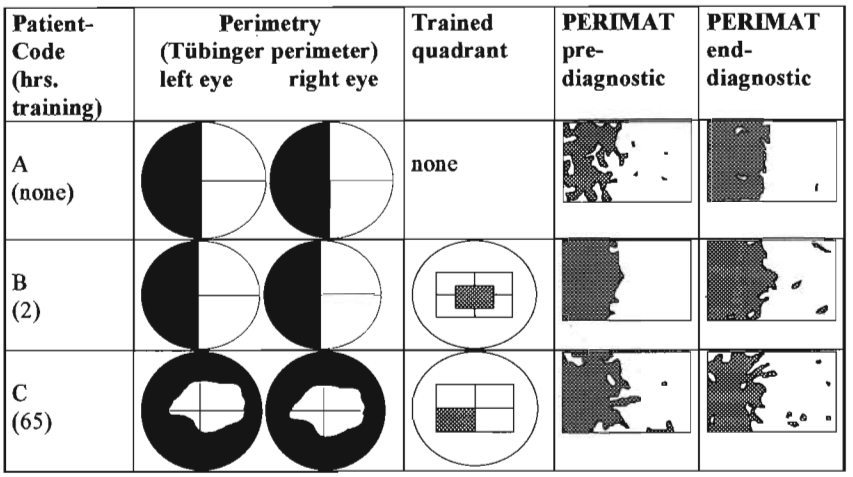

Fig. 3. Visual field size and training area of the three patients with little or no training. For explanation see legend to Fig. 2.

Follow-up investigations were made monthly, and if improvements were seen, the programs were adjusted accordingly by choosing smaller stimuli or a more sophisticated program level. While this procedure of individual adaptation to the patients performance introduces variability, it might maximize the improvement in individual patients.

In all patients, treatment was started with the VISURE program. As soon as the patients were able to perceive even the smallest possible stimulus, the SEETRAIN program was started. The patients had to exercise with a given software until they were able to detect more than 90% of the smallest stimuli at random positions on the screen. They were then asked to use the FORMTRAIN program where they either had to recognize different orientations of lines or the letters A, B, C and D. The COLORTRAIN program was given last. Due to the very prolonged time of our training procedure of several hundred hours, some patients discontinued the therapy prematurely. As a consequence, fewer patients completed the shape ($n = 8$) or color training sessions ($n = 7$).

2.7. Statistics

The normal population distribution was verified with the Kolmogorov-Smirnov tests ($P < 0.1$), but testing the homogenity of variance with the F-test showed little homogenity when comparing the group beginning the training within the first year to the other group beginning the training later. Therefore, instead of the parametric t-test, we analyzed some of our data with the Wilcoxon test. Because of the small number of subjects, we also pooled the data in a contingency table (≤ 100 h training vs. >100 h training, or $\leq 20\%$ increase vs. $>20\%$ increase) and applied a χ^2 test. The 20%-level was chosen because an analysis of the variability of measurements of visual field deficits in another study with 36 patients (Kasten, Wüst and Sabel, unpublished observations) had a baseline fluctuation of about 10% in their diagnostic PERIMAT test. With the 20%-level, we can be confident that a real increase beyond random variability had occured.

3. Results

3.1. Visual field enlargement

Several control procedures were introduced: (a) comparison of the treatment group vs. subjects with little or no therapy, (b) comparison of percent improvement of patients with minimal training vs. extensive training, (c) analysis of percent improvement over the baseline in relation to the number of training hours.

Compared to the baseline evaluation, nine of the 11 patients in the treatment group showed a visual field enlargement in the PERIMAT test with an average of 41.6%. The χ^2 test (1 d.f.) of the PERIMAT results revealed that the improvement was significant ($P < 0.01$; Table 3). Two patients experienced very little or no improvement: one was a stroke patient who exercised for 83 h, but this patient discontinued the therapy after having experienced a −19% deterioration in the performance in the PERIMAT program. Another patient, who had a tumor operation in the temporal and occipital lobe, experienced only a 7% improvement after 70 h of training. Both patients decided to discontinue the training because of lack of efficacy.

In the PERIFORM program and in the PERICOLOR program there were also improvements of 37.4% and 25.7%, respectively. As Fig. 4 shows, the extent of the improvement depended directly on the number of training hours. The χ^2 test showed a significant difference in the PERIFORM data ($n = 12$), but not in the PERICOLOR data ($n = 10$; Table 3).

In most patients, we found no increase within the first

Table 3
Contingency table for the χ^2 test of the results obtained with the diagnostic computer programs and the Tübinger perimeter

	Training (h)	
	≤100	>100
PERIMAT		
≤20% Improvement	5	1
>20% Improvement	1	7
PERIFORM		
≤ 20% Improvement	4	1
>20% Improvement	0	7
PERICOLOR		
≤20% Improvement	1	3
>20% Improvement	1	5
Tübinger perimeter		
≤10° Enlargement	6	3
>10° Enlargement	0	5

We pooled the patients with ≤20% improvement in the PERIMAT, PERIFORM and PERICOLOR programs in one group and the patients with >20% increase in the other group and subdivided the groups according to the number of training hours (≤100 h or >100 h).

We found a significant difference ($P < 0.01$) for the PERIMAT and the PERIFORM program, but not for the PERICOLOR program.

In the contingency table for the χ^2 test of the Tübinger perimeter, we pooled the patients with ≤10° enlargement of the visual field in one group and the patients with >10° enlargement in the other group, again subdividing the groups according to their number of training hours (≤100 h or >100 h); there was a significant difference ($P < 0.025$)

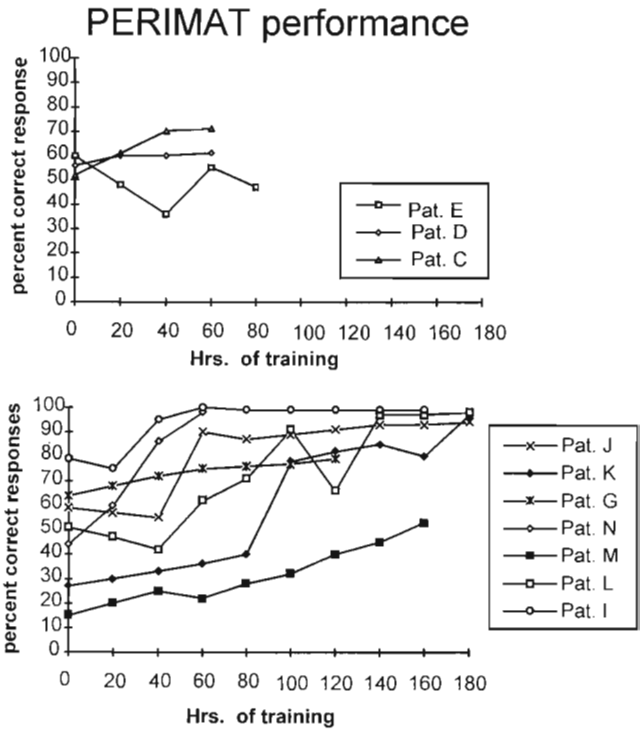

Fig. 5. Results of the monthly PERIMAT measurements of the patients. The upper graph shows the curves of three subjects with less than 100 h of therapy, the lower graph shows the data of the seven patients receiving more than 100 h of therapy training.

20 h of training in any of the tests. In the first monthly follow-up examination, five patients even had a decreased performance in the PERIMAT program (−4% to −9%). After an average of about 30 h of practice, however, an improvement, although unstable, was seen. With increased training of >100 h, the improvements became very obvious (Fig. 5). The correlation between

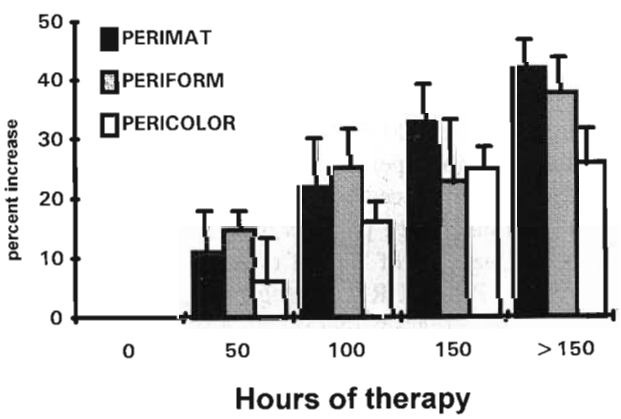

Fig. 4. Average percent increase (mean ± S.D.) after 50, 100, 150 and >150 h of training in the PERIMAT program ($n = 11$), the PERIFORM program ($n = 8$) and in the PERICOLOR program ($n = 7$).

percent improvement and number of training sessions was $r = 0.63$ in the PERIMAT, $r = 0.40$ in the PERIFORM and $r = 0.55$ in the PERICOLOR program ($P < 0.01$).

The qualitative analysis of the patients' performance revealed some important preliminary observations. Some patients (e.g. D, M) had an enlargement of the visual field only at the border between blind and intact visual areas. In other patients (e.g. J, N, L), the 'dissolution' of the blind areas started from islands of intact vision which are located within the blind parts of the visual field (Fig. 2). Interestingly, patients with large deficits such as complete homonymous hemianopia experienced 'border-enlargement'-type improvements, while patients with smaller deficits (i.e. quadrantanopia or scotoma) had improvement commencing in the regions of intact islands. Figs. 6, 7 display examples of typical patients with such different recovery dynamics.

As a follow-up, three patients were examined 6–12 months after the end of the treatment period. Their visual improvement was found to be stable; in some programs the patients showed no decrease, in others they had a loss of no more than −4% relative to the final outcome/measure immediately after the therapy, Fig. 8 shows the results for one of these three patients (J).

The three individuals, who practiced very little or not

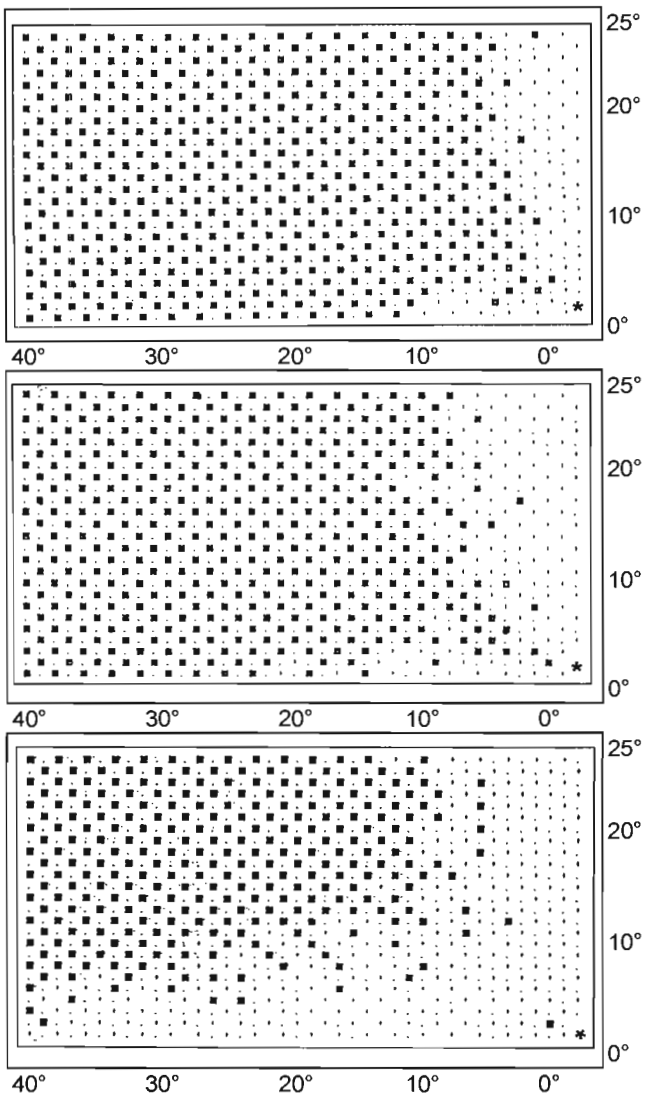

Fig. 6. PERIMAT results of the male patient M as obtained in January (upper panel), May (middle panel) and August 1991 (lower panel). Black squares indicate the undetected stimuli, and the star shows the position of the fixation point. The frame represents the edge of the computer monitor (40° horizontal and 25° vertical). One can see a reduced size of the blind area from January to August at the borderline of the blind field.

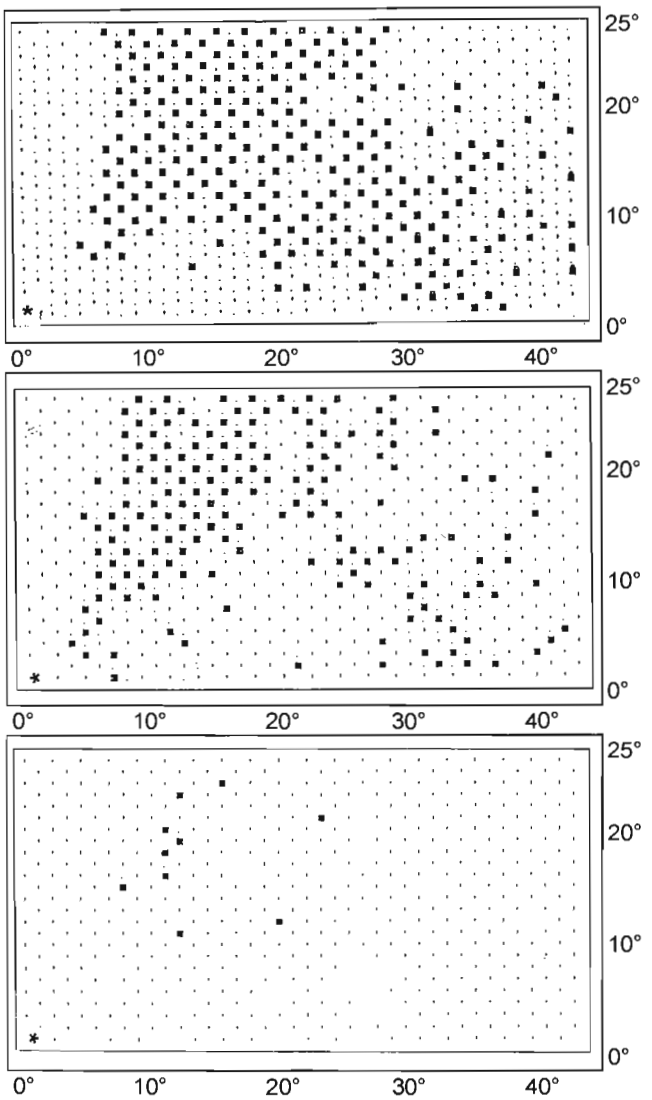

Fig. 7. PERIMAT results of the female patient L as obtained in October 1990 (upper panel), March (middle panel) and May 1991 (lower panel). For explanation see legend to Fig. 6. One can see an increased number of correctly detected stimuli, not only in the border area between the intact and the deficient field, but also well in the middle of the scotoma during the therapy.

at all, showed only improvements between 0% and 9% in the PERIMAT program. In the PERIFORM program, performance decreased by −9% and −27%. Unfortunately, with these patients no follow-up measurements were made with the PERICOLOR program. However, these results need to be interpreted cautiously because the three subjects in our second group were older than the treatment group. Analyzing the PERIMAT results in subjects with little or no training, we found a slight increase in the number of correctly recognized stimuli in the undamaged part of the visual field over time and a decrease in the damaged visual field. For instance, one patient (A) failed to detect 128 stimuli in the blind visual field and four stimuli in the healthy visual field during the first session. In the last examination 1 year later, she failed to see 154 items in the blind area and only one item in the healthy visual field.

The data of our independent measurements with the Tübinger perimeter and the results of a non-standardized interview with the patients about their subjective experience of improvement were less clear. Most patients showed an increased number of correctly perceived stimuli in the computer-assisted measurements and a reduced size of blind areas as shown by the Tübinger perimeter. Two patients with good improve-

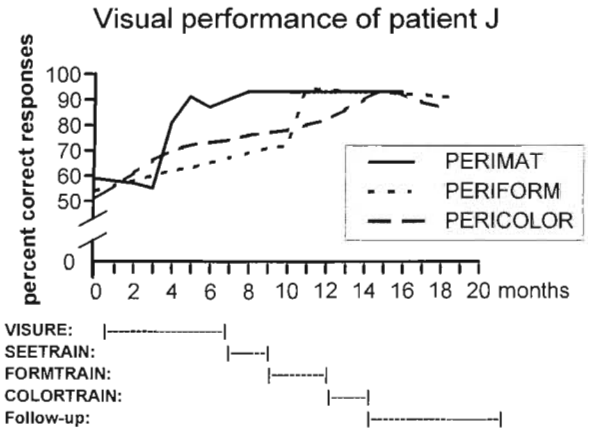

Fig. 8. Data from patient J. Following baseline assessment the patient trained for 8 months with the light detection task (VISURE and SEETRAIN), 3 months with the recognition of letters task (FORMTRAIN) and an additional 2 months with the discrimination of colors task (COLORTRAIN). After this 12 months of training several follow-up investigations were performed, demonstrating that performance remained stable after the end of the treatment in this patient.

ment in the PERIMAT program had only a small reduction of the blind parts as measured with the Tübinger perimeter. One male patient showed a remarkable increase in performance assessed by the computer programs as well as the Tübinger perimeter, but he did not report any improvements in vision, possibly due to his frustration with more than 200 h of training.

Dividing the patients in two groups (≤ 100 vs. >100 h training) and comparing those with a visual field enlargement of more than 10° or less than 10°, a significant difference was seen on the Tübinger perimeter data ($P < 0.025$ χ^2 test; Table 3). Although this analysis is nonsatisfactory because the deficits of four patients of the first group (≤ 100 h training) were larger than the visual field defects of most patients of the second group (>100 h training), the result is a useful indication that the visual field enlargement can be found not only by static perimetry in its central portion but also by dynamic measurements of the total visual field.

3.2. *Spontanous recovery vs. treatment effects*

Spontaneous recovery is known to occur within the first year after the injury. Therefore, we compared four of our patients who suffered brain lesion more than 1 year ago (maximum 20 years) with those who started training within the first year after injury. We found no significant difference between both groups in the PERIMAT, PERIFORM or PERICOLOR performance in the *t*-test ($P = 0.40$). The average increase of the first group ('old' lesions) was 27.6% (S.E. ±2.96%), the average improvement of the second group ('fresh' lesions) was 28.8% (S.E. ±4.92%). Furthermore, our three subjects of the second group with little or no therapy did not show any spontaneous recovery. This is compatible with the view that spontaneous recovery was not responsible for the improvements seen after training. It should be noted, however, that these three patients were older and had the most severe occipital lobe damage.

3.3. *Specificity of training effects*

To study the question of the specificity of light perception, shape recognition or color discrimination training, we performed a separate training of light perception (VISURE and SEETRAIN), shape recognition (FORMTRAIN) and color discrimination (COLORTRAIN). In the follow-up measurements, these functions were also examined separately with the computer-assisted diagnostic programs (Section 2.2). Training of light perception had a minor, but noticeable, influence on the ability to discriminate shapes (average 10% increase in PERIFORM) and colors (average 19% increase in PERICOLOR). Additional exercise of shape and color recognition resulted in a more pronounced improvement of these functions. There was a 20.5% increase in the diagnostic PERIFORM program. There was also an additional 11% increase in the PERICOLOR program during the COLORTRAIN training. In contrast to these results, during the FORMTRAIN exercises there was only a 2% increase in the PERICOLOR performance and a −1% decrease in the PERIMAT performance. Due to the COLORTRAIN program, there was an improvement of only 4% in the PERIFORM performance and of 2% in the PERIMAT performance (Fig. 9). These observations suggest that different training procedures have modality specific effects. But it is noteworthy that the shape recognition training with different letters (average of 23.3% improvement in PERIFORM) resulted in an increase similiar to that with the discrimination of lines of different orientations (17.8% improvement).

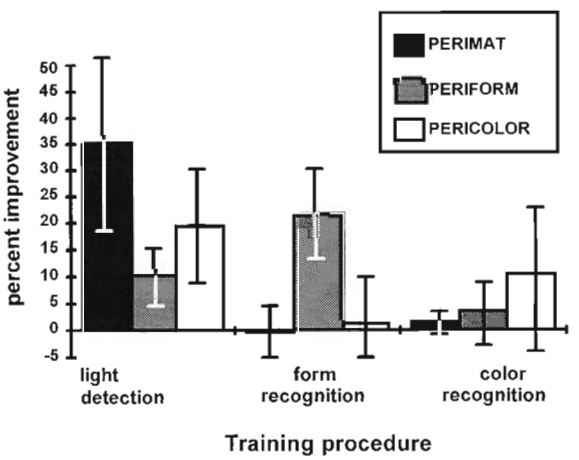

Fig. 9. Modality-specific improvement of visual functions. The left part of the graph shows the improvement in the diagnostic programs during the light detection training (VISURE and SEETRAIN). The middle part shows the improvement during the training with FORMTRAIN und the right part the improvement during the COLORTRAIN training (mean ± S.D.).

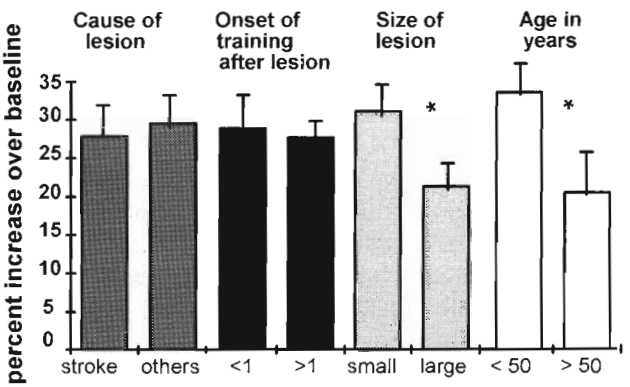

Fig. 10. Analysis of the variables influencing outcome. There is no significant difference between stroke and other causes (tumor operation, accident, bleeding) and no significant difference between the patients beginning therapy within the first year after the lesion or thereafter. We found significant differences between the younger group of patients (≤ 50 years) and the older group (>50 years), as well as between patients with small visual field deficits (scotoma, quadrantanopia) and large deficits (hemianopias). (Mean ± S.D.)

3.4. Variables influencing outcome

Finally, we correlated outcome (PERIMAT performance) with the time since lesion, the age of the patients, the initial size of the visual field deficit and the cause of the lesion. When stroke patients were pooled in one group and the other four patients in another group, no significant differences in outcome was found (t-test: $P = 0.45$; Wilcoxon test: $P = 0.47$). The comparison of the group with different onset of training (i.e. those beginning visual training within the first year after the lesion to those where training started more than one year later) revealed no significant differences (t-test: $P = 0.40$; Wilcoxon test: $P = 0.39$). However, two variables did influence outcome significantly; younger patients, under the age of 50 years, had better outcome than the group of patients >50 years (t-test: $P < 0.005$; Wilcoxon test: $P < 0.008$). Furthermore, patients with small blind areas (e.g. scotoma and quadrantanopia) had a considerably larger improvement (t-test: $P < 0.02$, Wilcoxon test: $P < 0.02$) than patients with larger blind areas (e.g. hemianopia, Fig. 10).

4. Discussion

This pilot study indicates that computer-based training may lead to a significant enlargement of the visual field in patients with partial injury of the visual system. The finding of significant improvement, despite a relatively small number of patients in each group and despite the heterogenity of the injury, argues for a powerful training effect. Training of light perception, shape and color recognition resulted in an improvement of visual performance of up to 71%; the extent of improvement depended on the number of training hours, the age of the patient and the initial size of the visual field deficit. Training appeared to be 'modality-specific', although some limited generalized effects (between modalities) were seen as well. The variables, 'time after lesion' and 'type of lesion', did not influence outcome. However, because of several methodological limitations, these results are only preliminary and conclusions should be regarded with caution. The conclusions are as follows:

(1) The trial did not contain a true placebo group (e.g. an attention or a fixation training).
(2) The patients were neither assigned randomly to a control or treatment condition, nor were the groups matched with respect to number of subjects, age or sex. In fact, the 'control' subjects in our second group were older than the experimental group.
(3) The lack of defined inclusion criteria considerably increased the variance in neuropsychological performance.
(4) Because the experimental design was not double-blind, experimenter bias cannot be ruled out. However, the diagnostic follow-up was performed automatically with computer programs which should have significantly reduced, or even eliminated, a potential experimenter bias.
(5) The conditions of the home training could not be standardized.
(6) Finally, the effects could be simply attributable to intervening variables such as long-term adaptation to the test situation and to the testing programs or improved attention or concentration.

Nevertheless, our training procedure improved visual functions in about 80% of our patients. The earliest improvement was seen after about 30 h of training. This observation is important because other investigators [4,19,24,25,47] trained their patients for a time period of less than 30 h, which might explain why they did not observe an enlargement of visual field borders of more than 6.7° eccentricity. Thus, in order to obtain improvement of visual function a prolonged period of training appears to be necessary.

The outcome of training depends on several factors such as the number of training sessions, age of the patient and the size of the visual field deficit. Our results are in agreement with the findings of Zihl [42] and Schmielau [36] who reported a small, but notable restitution of homonymous visual field disorders. Thus, they do not support the argument of Balliett et al. [2] that Zihl's findings may be an artefact of the dynamic measurements. In addition to dynamic diagnostic examinations with the Tübinger perimeter, we performed computer-assisted static diagnostic tests and still found a remarkable reduction of visual deficits. Our results also suggest that, contrary to long-held views [31], visual

field enlargement is possible even many years after brain damage. Hitherto, it was believed that at late post-lesion stages only compensatory strategies can help the patients. Our data rather point toward a notable plasticity of the nervous system, even many years after injury. In fact, patients who started their training very late after the lesion achieved scores similar to patients who suffered brain damage less than a year before training. In one case, marked improvements occurred in a patient who suffered damage as long as 20 years before starting training.

Since some patients began their training within the first few months after injury, spontaneous recovery may be responsible for improvements. It is known that spontaneous recovery can occur within the first few weeks or months after the lesions. Prosiegel [31] argues that a remarkable spontanous recovery of cognitive functions occurs only in the first 3–6 months after injury. Cramon and Zihl [6] reported spontanous recovery of vision in 12% of the patients during the first 6 weeks, while in the remaining patients improvements occurred during the first 6 months. Tiel-Wilk [40] reported an average spontaneous recovery of vision in stroke patients within the first 56 days. In our study, patients who started the training shortly after the brain damage had no better outcome than those who started several years after the lesion. Furthermore, our 'early treatment' group began the training 1–3 months after injury (i.e. at a time when spontaneous recovery should have already occurred). If the result of Tiel-Wilk [40] is correct, spontaneous recovery should have little, if any, influence on the performance. These considerations, when taken together, are compatible with the view that spontanous recovery of vision cannot explain our training-induced improvements. This is supported by the significant correlation between percent improvement and number of training sessions in the PERIMAT program (e.g. $r = 0.63$).

We also addressed the questions as to whether it is necessary to train different functional systems separately. In our study patients were trained separately with a light detection task that required them to discriminate shapes and colors (Fig. 9). As we have seen, when specific functions were trained (such as brightness perception) there are clear improvements in that specific function, but there are also some improvements in other functional systems. Whether such a generalized effect of training can occur has been controversial. For example, during the training of incremental thresholds, Zihl [42] found an improvement of other visual functions, e.g. the ability of color discrimination or visual acquity. In contrast, Schmielau and Potthoff [37] believe that each visual function such as light-detection, recognition of shapes or colors needs a specialized training procedure. Our results corroborate both opinions; while there are generalized effects, in that light detection training somewhat improves shape and color discrimination, the separate training of specialized functions appears to be of greater benefit. It is noteworthy that the training with different letters resulted in a similiar improvement than the training with lines of different orientations.

It also appears that brightness perception can be trained more easily than pattern or color discrimination. It has been suggested that subcortical structures such as the tectum may contribute to brightness perception [39], while line orientation is known to be analyzed by specific neurons located in 'orientation colums' within the neocortex [15]. In our patients the retinotectal pathway is presumably intact, while mainly the retino-geniculocortical pathway is injured, i.e. a stroke of the posterior cerebral artery damaged principally the optic radiation or the striate area. One might, therefore, expect brightness discrimination to be amenable to training more easily because the collateral pathway to the tectum is still intact. Alternatively, it is possible that visual functions, which are known to be controlled by specific brain circuitry, such as line orientation, also need to be specifically trained.

While this question cannot be answered satisfactory at the present time, a number of possibilities may be speculated upon which, in turn, might generate new experimental hypotheses. Our argument starts off with the presumption that the visual system in our patients has been only partially damaged and that the residual or recovered vision is mediated by the partially surviving primary system itself rather than function being 'taken over' by a distinctly different brain structure.

This assumption appears reasonable for the following two reasons; firstly, improvement of vision is more easily obtained when patients have a smaller lesion (see Results, Section 3), and, secondly, visual field enlargement 'starts' in many of our patients from islands of intact vision (see discussion below).

Given this assumption, there are two alternative explanations why training induces enlargement of visual field borders. The first explanation is based on the assumption that the remaining system is 'static', without any major changes in the function of its elements. Here, the system would 'learn' to use latent or alternative structures. Or, alternatively, the system undergoes active, 'dynamic' changes, which are an expression of an underlying plasticity of the surviving elements in the vicinity of the lesion (in the optic radiation or in the visual cortex).

For the purpose of discussion, we include in the 'static' processes any events which do not require fundamental structural or functional changes in the surviving neuronal elements in the vicinity of the lesion or in the deafferented structure. Rather, the remaining brain only makes better use of the existing pathways. For instance, it is conceivable that due to our training the patients learn to focus their attention in the direction of the blind areas and, thus, make better use of the limited

information which can still be obtained with the surviving neurons of the partially damaged visual system. We reported the data of three patients with little or no therapy and found no improvement. The brain may rely only on the information from the 'intact' parts of the visual field and may neglect the small input of the damaged areas (similarly to what happens in amblyopia during development). Thus, due to the training, the brain somehow makes better use of the small perception capacities within the hemianopic field, without requiring structural changes.

'Dynamic' changes, in contrast, are those where the surviving elements of the partially damaged system itself undergo some compensatory physiological changes. It is known that animals undergo dramatic spontaneous recovery after injury to most functional systems [9–11], including the visual system [33–35]. If we want to better understand the events underlying training-induced functional improvements, we first need to consider the 'dynamic' post-lesion changes which occur spontaneously.

4.1. Receptive field reorganization

Following deafferentation, the receptive fields in target structures undergo massive reorganization. This observation goes back to studies of the primary motor and sensory cortex following the removal of a nerve or a digit.

Kaas et al. [17] and Zarzecki et al. [41] observed an enlargement of receptive fields in somato-sensory cortex following deafferentation by digit removal in racoons. It was speculated that this may be due to enhanced effectiveness of existing cortical synapses or synaptic proliferation.

Reorganization in the visual system was first reported by Eysel [7]. Since then, the studies of Gilbert and Wiesel [12,13] revealed neurons with long distance projections in the visual cortex that might comprise the biological substrate of receptive field reorganization, changes which can happen very rapidly after injury [14]. Also, 5–10° lesions of the retina in adult mammals markedly altered the representation of the retina in primary visual cortex [17,18]. Cortical neurons that normally have receptive fields in the lesioned region of the retina acquired new receptive fields in portions of the retina surrounding the lesions.

Receptive field enlargements in the visual system do not only occur in distant, deafferented targets but they have also been seen at the border of visual cortex damage [8,21]. It is currently not known if these or similar receptive field changes contribute to recovery of visual function in animals or patients, an issue which needs to be investigated more in the future.

4.2. Up-regulation of function in surviving elements

According to another working paradigm adopted in our own laboratory [34,35,38], the surviving cells of the damaged system itself alter their function and, thus, contribute to the restoration of function (see also the discussion of 'sub-total lesions' by Finger [9,11]).

The clinical data presented here are consistent with both theories of recovery. Patients with large visual field deficits (e.g. complete hemianopia) experienced improvements which progress gradually from the border of the intact field into the blind area. Here, an enlargement of the intact receptive fields at the borderline is a conceivable, yet unproven, physiological mechanism. Fig. 6 shows the data of patient M in which the improvement was first seen at the border region, moving gradually into the blind field. Here, we found a significant increase of correctly detected stimuli in the PERIMAT program after about 100 h of training. Thereafter, no further improvement occurred, even though patient M continued training for another 100 h. It is conceivable that the receptive field expansion at the border reached its maximum after 100 h, or that the maximum up-regulation potential was achieved.

Patients with smaller lesions (scotoma or quadrantanopia) had small islands of intact vision in the blind sectors when first assessed prior to training. Fig. 7 is an example of such a case. During training, we found an enlargement of these islands of vision in addition to the expected improvements which start at the border between the intact and the blind visual field. These observations are in agreement with the theory that training-induced recovery may involve partially injured neuronal system which undergo a reactivation or reorganization. If our speculations are correct, we would predict that the selective training of these islands of residual vision might be more effective therapy than random stimulus presentation throughout the blind visual field. This can be tested experimentally in future studies.

In summary, we conclude that the treatment of visual deficits with home-based computer training improves visual functions. This also appears to be an effective approach when the lesion is many years old, supporting the concept of late rehabilitation training (see also Bach-y-Rita [1]). A double-blind, randomized, controlled trial is now underway to validate this therapeutic approach to restore vision in patients with partial deficits using economical computer-based home training under standardized conditions.

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