

Computer-Based Training of Stimulus Detection Improves Color and Simple Pattern Recognition in the Defective Field of Hemianopic Subjects

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Abstract

■ In a previously conducted randomized placebo-controlled trial, we were able to demonstrate significant visual field enlargement induced by restitution therapy in patients with cerebral lesions [Kasten, E., Wuest, S., Behrens-Bamann, W., & Sabel, B. A. (1998c). Computer-based training for the treatment of partial blindness. *Nature Medicine*, 4, 1083–1087.]. Visual field training was performed on a computer monitor for 1 hr per day over a period of 6 months. Since the procedure included only stimulation with white light, in the present study we investigated if this simple detection training had a transfer effect on color or form recognition in the trained area (i.e., in the absence of modality specific training). Answering this question would be crucial for planning optimal restitution therapy: In case there is no transfer of training effects to other visual modalities, a specific treatment of each visual function must be performed in order to achieve maximum benefit. Therefore, we analyzed the data from 32 patients with visual field defects who had participated in the original trial and whose form and color recognition had been investigated. The experimental group ($n = 19$, restitution training) experienced not only an increase of 12.8% correctly detected stimuli (PeriMa program, $p < .05$), but also an improvement of 5.6% in

pattern recognition (PeriForm) and of 6.1% in color perception (PeriColor), respectively. In contrast, the placebo group ($n = 13$, fixation training) showed no significant changes from baseline to final outcome in any of the visual modalities (PeriMa: 0.3%; PeriForm: -0.3% ; PeriColor: 0.4%). Conventional perimetry yielded an increase of 7.8% detected stimuli in the experimental group, but only of 1.2% in the placebo group ($p < .05$). For form recognition and color perception, the differences between the results of the experimental and the placebo groups narrowly missed significance. However, correlations of diagnostic results showed that mainly those patients who had achieved visual field enlargement also improved in color and form perception: $r = .67$ ($p < .05$) between PeriMa and PeriForm and $r = .32$ between PeriMa and PeriColor. We conclude that visual restitution training using a simple white light stimulus has at least some influence on improving other visual functions such as color and pattern recognition. This result supports the “bottleneck theory” of visual restitution, i.e., training effects can be explained as a process of perceptual learning and increased processing of information by residual structures surviving lesions of the primary visual pathways. ■

INTRODUCTION

Patients suffering from impaired vision commonly experience many limitations in their activities of daily living such as deficits in visual orientation or detection of objects in visual space. Brain injury bears an evident risk of inducing visual deficits, because the visual pathways traverse the entire brain, and several cerebral regions, located in parietal, frontal, and temporal lobes, as well as subcortical structures, are more or less involved in visual information processing. Consequently, the probability of acquiring a visual field defect after stroke, trauma, or brain surgery is as high as 20–30%.

One would assume that the problems caused by visual impairments should have led to a vigorous effort of designing treatment strategies. Yet, this has

not been the case. The concept that the adult visual cortex is strictly organized (e.g., in topographical units) and possesses a high degree of specificity led to the assumption that visual field loss is irreversible. Nevertheless, in recent years, we have witnessed a paradigm shift in neuroscience, namely that the brain is able to compensate for lost functions (see, e.g., Bach-y-Rita, 1990; Finger, LeVere, Almlie, & Stein, 1988). Even the visual system, previously considered to be hard-wired both in animals and humans, has proven to possess a remarkable flexibility in adapting to damage (see, e.g., Chino, 1999; Sabel, 1999a,b; Werth & Moerenschlager, 1999; Kasten, Wuest, Behrens-Baumann, & Sabel, 1998c; Gilbert, Das, Ito, Kapadia, & Westheimer, 1996; Gilbert, 1998; Pöppel et al., 1987; Eysel, 1976; Eysel & Grüsser, 1978; Eysel & Schmidt-

Kastner, 1991; Eysel, Eyding, & Schweigart, 1998; Eysel et al., 1999).

To determine if improvement of vision may be achieved even beyond the time window of spontaneous recovery (which is usually on the order of weeks to some months), we recently conducted two prospective, randomized, placebo-controlled clinical trials with 38 patients who sustained visual system injury. In this study, we demonstrated that a computer-based visual restitution training can significantly enlarge the visual field after damage (Kasten et al., 1998c). Patients were randomly assigned to an experimental (treated with restitution training) or a placebo group (provided with foveal fixation training only). Restitution treatment consisted of a PC-based training program, which the patient performed at home for 1 hr daily over a period of 6 months, i.e., about 150 hr of training. During this time, several thousand visual stimuli were presented systematically on the computer monitor so that stimulation of areas of residual vision located between the intact and the blind visual field sector ("transition zone," see Kasten, Wuest, & Sabel, 1998a) was achieved. While most patients in the placebo group experienced no change in visual field size, the experimental group displayed a reliable visual field enlargement as revealed by a significant shift of the visual field border and by improvements in the detection of small visual stimuli (Kasten et al., 1998c).

From these findings, the question arose whether training with simple white stimuli also has a transfer effect on form and color recognition as well, even if these functions were not specifically trained. This question has both theoretical and practical implications. From a practical point of view, it is important to know if form and color perception need to be trained separately. This question is significant because our restitution training requires considerable time. In many patients, we found that the first signs of visual field enlargement occurred only after 2 or 3 months of training, i.e., between 50 and 100 hr of practice. Therefore, specific training of additional visual functions such as form recognition and color perception would likely require a considerably longer time in order to achieve improvement of these functions. On the other hand, if training limited to simple stimulus detection has transfer effects, a specific treatment of color or form perception may not be necessary.

From the theoretical point of view possible transfer effects would provide some insight into the neural mechanisms underlying the improvements of visual functions following training. In agreement with Eysel et al. (1999) and Wörgötter, Suder, and Funke (1999) who found a considerable plasticity of receptive fields within the visual system, we propose that the training-induced improvement may be explained by an enlargement of isolated receptive fields in the border area of the blind sector. If this hypothesis is correct, the en-

largement may lead to a loss of visual acuity in the restored area, because those isolated receptive fields have to process additional visual information obtained from surrounding areas. Thus, an exact investigation of pattern recognition in the trained area can either support or refute this hypothesis.

The present study was, therefore, conducted to gain a better understanding of the influence of (nonmodality specific) visual detection training with simple white dots on dark background on the patients' ability to recognize colors and simple forms in the transition zones. Because these data were collected as part of the randomized placebo-controlled clinical trial, which has previously been reported, any findings would definitively resolve the issue of whether simple detection training transfers to other visual functions and, thus, provide new insight into mechanisms of postlesion plasticity.

RESULTS

Originally, 38 patients were included in the two studies (Kasten et al., 1998c). However, since not all of these patients were also tested for color and form perception, we only analyzed the data of 32 subjects with a complete diagnostic data set (for the description of subjects, see Methods). Due to the reduced number of patients, our current results showed some differences in comparison to our data, which were originally published in 1998 (Kasten et al., 1998c). Now, the experimental group experienced a significant increase in the number of correctly detected stimuli using high-resolution campimetry (PeriMa pre-post difference: $12.8 \pm 2.6\%$), as well as in conventional perimetry (TAP-2000: $7.8 \pm 2.5\%$) after training with simple white stimuli presented on dark background. We now also report an improvement in pattern recognition (PeriForm: $5.6 \pm 1.6\%$) and color discrimination (PeriColor: $6.1 \pm 2.1\%$) in the trained area of the defective visual field, even though these functions were not specifically trained. In contrast, without stimulation of the visual field border, the placebo group

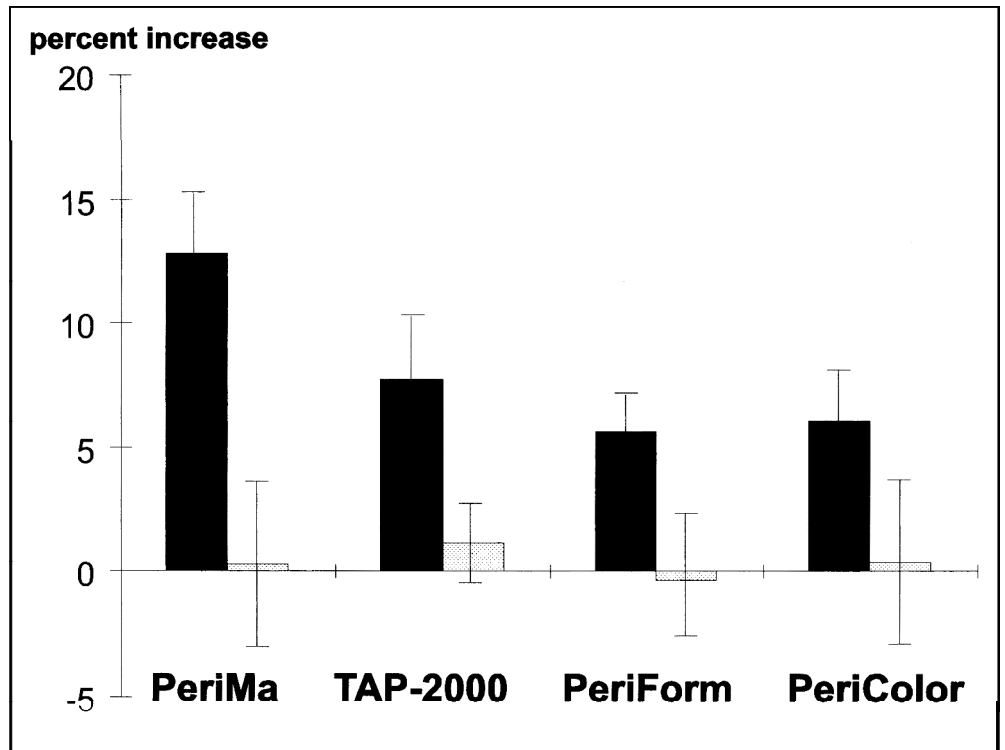
Table 1. Comparison of Perimetric and Campimetric Results Between Experimental and Control Subjects

	<i>Experimental Group Average of Pre-Post Difference</i>	<i>Placebo Group Average of Pre-Post Difference</i>	<i>t test</i>
PeriMa	$12.8 \pm 2.6\%$	$0.3 \pm 3.4\%$	$p < .01^*$
PeriForm	$5.6 \pm 1.6\%$	$-0.3 \pm 2.7\%$	$p = .06$
PeriColor	$6.1 \pm 2.1\%$	$0.4 \pm 3.1\%$	$p = .12$
TAP-2000	$7.8 \pm 2.5\%$	$1.2 \pm 1.4\%$	$p < .04^*$

Statistical analysis with Student's *t* test showed significant differences for the PeriMa detection task and the TAP perimetry, but not for PeriForm and PeriColor data.

* $p < .05$.

Figure 1. Average changes in perimetry and campimetry following computer-based restitution training. Black bars indicate the changes of the restitution group, gray bars those of the placebo group (mean \pm SE). PeriMa is a high-resolution detection task, TAP-2000 is conventional perimetry on a hemispheric perimeter, PeriForm is a high-resolution form campimetry and PeriColor is a high-resolution color campimetry. Significant differences between the experimental and the placebo group were found for PeriMa and TAP data ($p < .05$), for PeriForm and PeriColor only a trend could be shown.



showed no such significant changes between pre- and posttraining measures (PeriMa: $0.3 \pm 3.4\%$; PeriForm: $-0.3 \pm 2.7\%$; PeriColor: $0.4 \pm 3.1\%$; TAP: $1.2 \pm 1.4\%$).

A *t* test (see Table 1) between the experimental and the placebo group was significant for PeriMa results ($p < .05$) and for TAP-2000 perimetry ($p < .05$). PeriForm narrowly missed significance ($p = .057$), PeriColor was not significant but had a clear tendency ($p = .12$). Figure 1 shows the percent increase between the results of the baseline investigations and the final outcome of the three high-resolution programs and TAP-2000 perimetry.

As observed in our previous double-blind study, visual field enlargement in patients with lesion of the optic nerve was much higher than in the group with postchiasmatic damage as far as simple stimulus detection was concerned. Although interestingly, this was not the case for form and color perception: Improvement was smaller with a higher variance in both groups of patients receiving restitution training. Table 2 shows the detailed results.

If the enlargement of visual field size, measured with the PeriMa light detection task, has generalized effects on the recognition of colors and forms, the correlation between the increases in the different visual tests must be high. We checked this by calculating the Pearson's correlation coefficient between the results of the campimetry on the computer screen and the conventional TAP perimetry, which was found to be significant ($r = .52, p < .05$). In addition, we also found high correlation coefficients between PeriMa

and PeriForm ($r = .67, p < .05$) and between PeriMa and PeriColor ($r = .32, n.s.$). Likewise, the correlation between PeriForm and PeriColor was significant ($r =$

Table 2. Comparison of Training Results Between Patients with Optic Nerve Lesion versus Postchiasmatic Damage

Experimental Group	Patients With Optic Nerve Damage (n = 9)	Patients With Postchiasmatic Damage (n = 10)
PeriMa	19.8 \pm 3.6%	6.5 \pm 2.5%
TAP-2000	12.6 \pm 3.8%	1.8 \pm 0.9%
PeriForm	5.7 \pm 2.5%	5.5 \pm 2.3%
PeriColor	2.3 \pm 3.0%	9.6 \pm 2.6%
Placebo Group	Patients With Optic Nerve Damage (n = 8)	Patients With Postchiasmatic Damage (n = 5)
PeriMa	6.3 \pm 2.1%	-9.4 \pm 6.1%
TAP-2000	2.3 \pm 2.1%	-0.5 \pm 1.0%
PeriForm	3.4 \pm 2.5%	-6.2 \pm 5.1%
PeriColor	4.6 \pm 3.4%	-6.4 \pm 4.7%

Visual field enlargement was most pronounced in the optic nerve experimental group. Interestingly, the improvement of color recognition was stronger in the postchiasmatic damaged experimental group than in the group with optic nerve injury (mean \pm SE).

.37, $p < .05$). Therefore, we conclude that patients who showed an enlargement of the visual field as a result of training using a simple white stimulus also produced an increase in the ability to perceive colors and forms in the regained visual area.

In a second analysis, the shift of the border between intact and defective areas of the visual field was investigated. The position of the visual field border between the deficient and the intact region was examined by measuring the horizontal distance from the vertical meridian at five positions (description see below). Unfortunately, our previously used method of measurement turned out not to be optimal. Especially in patients with lesions of the optic nerve, we often found intact areas behind a scotoma, which were not included in our previous determined calculating. Therefore, the results may underestimate the real enlargement of the visual field. In the experimental group, the average shift of the

borderline was $3.8 \pm 1.0^\circ$ in PeriMa results and $1.7 \pm 0.6^\circ$ in PeriForm and PeriColor. In the placebo group, we only found an average change of $2.9 \pm 1.2^\circ$ for PeriMa results, $1.0 \pm 0.7^\circ$ in PeriForm, and $0.02 \pm 0.5^\circ$ in PeriColor.

Also interesting are the relative positions of the boundary itself. Figure 2 shows the shift of the border between intact and defective areas during therapy. The experimental group showed a clear shift of the border into the direction of the blind area in all tests of visual functions. In contrast, the placebo group exhibited inconsistent changes of the visual field border across the three tested functions and different eccentricities.

We only trained patients with a stable baseline. Therefore, the correlation coefficient between the time interval since lesion and increase in high-resolution perimetry (HRP) was small and not significant (PeriMa:

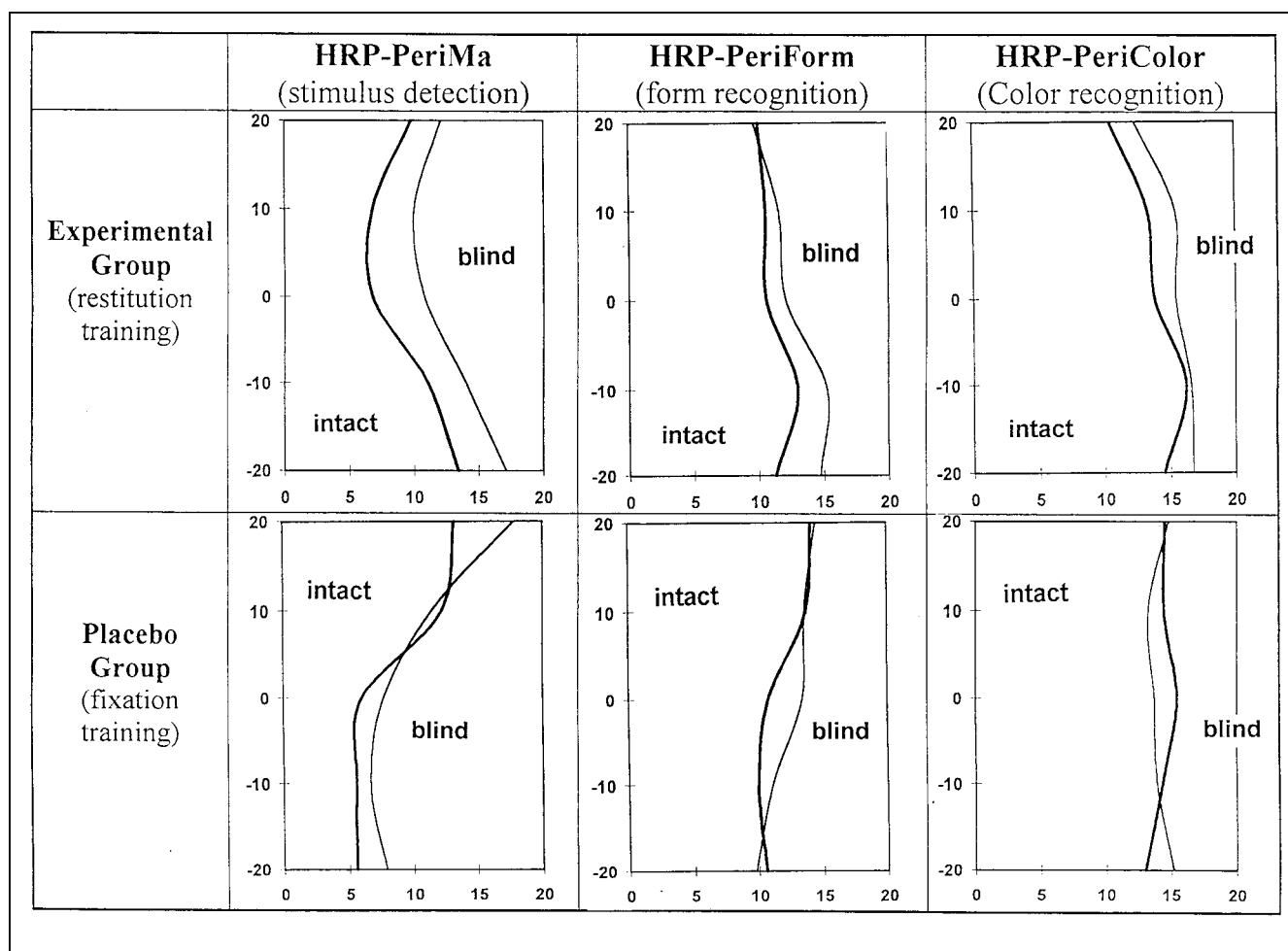


Figure 2. Qualitative changes of visual field border in experimental versus placebo groups on the basis of measurements described in Figure 1. We calculated the average positions of the border between intact and deficient visual field. The x and y axis indicate horizontal and vertical eccentricities (degrees of visual angle). The solid line indicates the borderline before training and the thin line after the therapy. For this analysis, all field defects were transferred to the right hemisphere so that the intact part of visual field is always on the left side of each picture and the defect side is always on the right side. While the experimental group (upper three panels) showed a clear border shift into the direction of the blind area in all three visual functions (detection, form, and color recognition), the placebo group exhibited inconsistent border shifts, showing sometimes increases and sometimes decreases.

$r = .25$, *ns*). Therefore, spontaneous recovery seems to have less responsibility for the increase.

Since we had found in our previous pilot study (Kasten & Sabel, 1995) that the size of the defective area and the amount of increase due to the training procedure are closely related, we again tested if these variables correlate. However, in the current study, there was only a small correlation between the blind visual field size and the degree of improvement (PeriMa: $r = -0.3$; TAP: $r = -0.25$, both *ns*).

In addition, in the current data, we could not reproduce earlier results pointing to an effect of age on visual field enlargement that had been observed in our first pilot study. Age and visual field enlargement were unrelated (PeriMa: $r = -0.06$; PeriForm: $r = .25$; PeriColor: $r = .02$; TAP: $r = -0.7$). However, one may consider that very young and very old age was an exclusion criteria (see Methods).

DISCUSSION

A topic of controversial discussion has been whether training in a detection task using simple stimuli can influence other nontrained functions such as shape and color recognition. Training of incremental thresholds (Zihl, 1980) does appear to produce improvements in other visual functions, e.g., the ability to discriminate colors, as well as visual acuity, while other researchers have reported that each visual function, such as light detection, recognition of shapes, and perception of colors, must be trained separately and that no transfer occurs (Potthoff, 1995; Schmielau, 1989).

We had addressed this problem in our first pilot study (Kasten & Sabel, 1995). In addition to training of light perception, specific treatment of shape recognition and color discrimination was performed in 11 patients. Detection training with simple white stimuli produced minor, but noticeable, improvement of color and shape discrimination as well. Additional treatment with specific shape or color recognition training resulted in a more pronounced improvement of those functions. Thus, when specific visual abilities were trained (such as brightness perception), the resulting improvements transfer to other visual functions, although specific training appears to be most beneficial. Therefore, the results of our first pilot study corroborated 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. However, it should be kept in mind that this first pilot trial was neither double-blind nor sufficiently placebo-controlled and comprised only a small sample of 11 patients. In order to get a more reliable decision from the present trial, we specifically analyzed our data with regard to transfer of training benefits to other functions.

To summarize our results, we clearly found mostly significant transfer effects of the simple training of light detection on the recognition of forms and colors. However, the improvement in the latter two functions (PeriForm and PeriColor, about 6%) was not as high as in detection tasks applied in this study (PeriMa: 13%; TAP-2000: 8%). The average enlargement of visual field found in this study was smaller than what we had observed previously. The restitution group experienced an increase of 3.8° in the light detection task, 1.7° for form, and 1.7° for color recognition, respectively, in the trained area of the defective visual field. Note that our method of measurement underestimated the real amount of border shift, because peripheral improvement behind central blind areas was not taken into account; a problem that was especially relevant in patients with lesions of the optic nerve.

Secondly, our computer-based training procedure allowed only the stimulation of a central area representing a large amount of brain tissue in the striate cortex (see cortical magnification factor, e.g., Daniel & Whitteridge, 1961). Therefore, in central parts of the visual field, any training success, expressed as degrees of visual angle will be more difficult to achieve than in the periphery that has larger receptive fields and is represented by less tissue in the occipital lobe. Consequently, an enlargement of a few degrees of visual angle in the central area implies a restitution of a considerably greater area of neuronal tissue in the striate area than a comparable shift in the peripheral parts. From this point of view, a presumably "small" increase of only 3.8° average visual field enlargement can be a great success for the patient and may lead to considerable improvements in everyday life.

Additionally, the high correlation coefficients between the increases of light detection and color/form recognition showed that in patients in which the training procedure was effective with respect to an enlargement of the visual field border, we also found an improvement of form and color recognition. This result again supports the conclusion that transfer effects exist between the different visual modalities.

Thus, the results of the present study confirm that an unspecific computer-based stimulus detection training has a generalized effect on other visual capacities as well, though not in an optimal fashion.

The information of color, motion, and shape of an object is believed to be processed separately in the parvo- and magnocellular system (Leonards & Singer, 1997; Meissirel, Wilker, Chalupa, & Rakic, 1997; Moller & Hurlbert, 1997; Steinman, Steinman, & Lehmkuhle, 1997). However, the findings of many investigations, e.g., on the basis of event-related brain potentials, suggest that when color and shape are easy to discriminate, they are identified and selected in parallel (Moutoussis & Zeki, 1997; Smid & Heinze, 1997; Smid, Jakob,

& Heinze, 1997; van-der-Velde & van-der-Heijden, 1997). However, because each stimulus possesses not only luminance, but also form and color (Cohen, 1997), one may argue that any training of stimulus detection must have some influence on form and color perception (Syrkin & Gur, 1997). It has been suggested that subcortical structures, such as the tectum, may contribute to brightness perception, while line orientation is known to be analyzed by specific neurons located in "orientation columns" within neocortex (see, e.g., Hubel, Wiesel, & Stryker, 1979). Therefore, one might predict that brightness perception can be trained more easily than pattern or color discrimination. In our patients, the retino-tectal pathway was presumably intact, whereas the retino-geniculo-cortical pathway was compromised. One might expect brightness discrimination to be more amenable to training because the collateral pathway to the tectum is still intact. In contrast, color and, particularly, form recognition, are not believed to be mediated by subcortical structures, but by higher cortical areas (e.g., "blobs" and "interblobs" in V1, V2, V3, V4, and V5). Therefore, the result that not only an increase of stimulus detection had been found, but also an improvement of form and color recognition, supports the theory that the training does not primarily stimulate the subcortical pathway, but implies a real restitution of cortical functions.

Table 1 shows that patients with lesions of the optic nerve achieved much larger improvement than the group of subjects with postchiasmatic damage in the simple detection task, while even the optic nerve placebo group showed an increase that was comparable to that of the postchiasmatic experimental patients. These results certainly need an explanation. In contrast to the postchiasmatic patients, who suffered from homonymous visual field deficits on both eyes, many of the optic nerve patients had an intact and an injured eye. We hypothesize that in daily life, the latter group exhibits a strong tendency to use only the better eye and to neglect the weak information arising from the damaged eye. This disuse leads to a further degeneration of the defective eye. During the training sessions, the intact eye was always covered so that the patients were, thus, forced to use their weak eye. Even in the placebo condition, they had to learn to use the deficient eye again. This seems to lead to an improvement with every kind of stimulus, which may explain the increase in visual performance in the optic nerve placebo group.

It was hypothesized that the visual field increase is based on an enlargement of single receptive fields within the border area of the blind field (Kasten et al., 1999c). However, such receptive field enlargements should lead to a restricted visual acuity in the trained area because information arising from adjacent parts of retinal tissue would have to be processed by the same neuronal population. This should result in lower

visual resolution and contrast. If this theory is true, at least the form recognition in the trained areas should have been stable or decreased after the training. This was not the case, in contrast, we found a small increase in pattern recognition and of visual acuity (Kasten et al., 1998c). It is therefore conceivable that the effects of the training are not enlargements of receptive fields, but rather their refinement or restriction, thus, producing less "white noise" and sharper information processing.

In another article, we had proposed a "bottleneck theory" of the damaged visual system (Kasten, 1999b; Sabel, 1997). The striate area V1 sends its information to many other visual areas such as V2, V3, V4, and V5, which, for instance, are involved in color and form recognition (Bartolomeo, Bachoud-Levi & Denes, 1997; Hurlbert, 1997; Ishii, Kita, Nagura, Bando, & Yamanouchi, 1992). As mentioned above, in most of our patients, we only found a lesion in the section between the optic nerve and the striate area, but, normally, no damage was seen within higher visual areas. Therefore, the lesion produces a "bottleneck" for visual information to proceed to higher cortical areas. Therefore, if the flood of information through this bottleneck can be increased, the analysis of colors and forms within the higher cortical areas is normally guaranteed.

We propose that isolated intact neurons in those higher-order areas of the visual system in daily life do not receive enough sensory information or input to produce a conscious perception, especially because there is a considerable inhibition from the neighboring intact regions. The existence of such residual functions has been shown in several studies, demonstrating areas with residual visual capacities as "transition zones" and "visual islands" within the blind field (Kasten et al., 1998a; Wessinger, Fendrich, Ptito, Villemeure, & Gazzaniga, 1996; Wessinger, Fendrich, & Gazzaniga, 1997; Wessinger, Fendrich, & Gazzaniga, 1999). Most patients focus their attention on the information that arises from intact visual field regions, and they neglect the small and perhaps confusing imprecise perception that originates from the damaged area. We propose that our training procedure forces the patients to focus their attention on this weak stream of information arising out of the transition zone, because the intact field was kept in darkness (which also reduces the influence of lateral inhibitory interactions). In this manner, the patients gradually learn to process this visual input and to get a conscious impression of the specific part of the environment, which is projected onto the transition zone. By passing this bottleneck, the information now can reach higher cortical areas again (e.g., V2, V3, V4, or V5), leading to an adequate processing of modality specific functions so that form or color recognition become possible.

Future research should address the question if it is possible that visual functions, such as line or color recognition, will show more pronounced increases following a specific restitution therapy compared to our simple detection training. This and similar issues will help us to improve the efficiency of visual restitution training to the benefit of many patients suffering from visual field defects.

METHODS

Subjects

We investigated 32 patients, 12 female and 20 male, average age 51.1 ± 2.6 years (mean \pm SE). The cause of the visual deficits were: (1) vascular diseases (e.g., stroke, cerebral hemorrhage, insufficient blood circulation, $n = 9$); (2) trauma or brain surgery ($n = 13$); or (3) cerebral inflammation and other lesions ($n = 10$). All patients had either a postchiasmatic damage causing a homonymous visual field defect ($n = 15$) or a lesion of the optic nerve resulting in heteronymous visual field defects ($n = 17$).

Exclusion Criteria

All patients had been screened for a number of exclusion criteria: age below 18 or above 75 years, other visual diseases (e.g., lesions of the eye, reduced foveal visual acuity, color blindness), nystagmus, visual neglect, motor deficits (e.g., hemiplegia), cognitive deficits (e.g., serious sustained attention or impaired memory), or psychotic mental diseases (e.g., depression). Because spontaneous recovery is known to occur within the first year after brain lesion (Gray et al., 1989; Messing & Gänshirt, 1987; Zihl & von Cramon, 1985, 1986; Kölmel, 1984, 1988; Bogousslavsky, Regli, & van-Melle, 1983; Hier, Mondlock, & Caplan, 1983; Trobe, Lorber, & Schlezinger, 1973), only patients whose lesions were older than 1 year (mean: 7.0 ± 1.7 years; minimum: 1, maximum: 50 years) were selected for the study. Additionally, each patient's drug history was explored in detail before the examination, because several drugs influence visual field size through pupil dilation (Henson

& Morris, 1993; Flammer & Niesel, 1984). There were no significant differences between the experimental and the placebo group. Table 3 shows the data for each group separately.

Randomization

Data for this study were acquired in two independent trials from patients with postchiasmatic lesions or damage of the optic nerve. In both trials, identical training methods were used, and subjects were assigned randomly to either the experimental or the placebo group. Originally, 38 patients were included in the two studies (Kasten et al., 1998c). However, since not all of these patients were also tested for color and form perception, we only analyzed the data of 32 subjects with a complete diagnostic data set.

Diagnostic Procedures

All diagnostic examinations were done under constant luminance conditions in all sessions. Moreover, standardized instructions for each patient were presented on the monitor at the beginning of each program. Perimetry and all computer-based campimetric programs were carried out with a head/chin support to provide for a stable head position. Patients were allowed to use their eyeglasses during examinations.

The total size of each eye's blind area was determined by static monocular perimetry using a Tübinger Automatic Perimeter "TAP-2000" (30° visual field, threshold-oriented perimetry, 191 stimuli, presentation time: 200 msec, interval time: 900 msec; for a description of the TAP-2000, see, e.g., Lachenmayr & Vivell, 1992). Fixation was controlled with a video camera and catch trials.

Additional visual diagnosis was done with a set of computer-based programs presented on a 17-in. cathode ray tube (CRT, 72 Hz). These programs have been used for the investigation of visual abilities in brain damaged patients in some previous studies (Sabel, 1997; Sabel, Kasten, & Kreutz, 1997; Sabel & Kasten, 2000; Kasten, 1994; Kasten, Wiegmann, & Sabel, 1994;

Table 3. Description of the Patient Sample

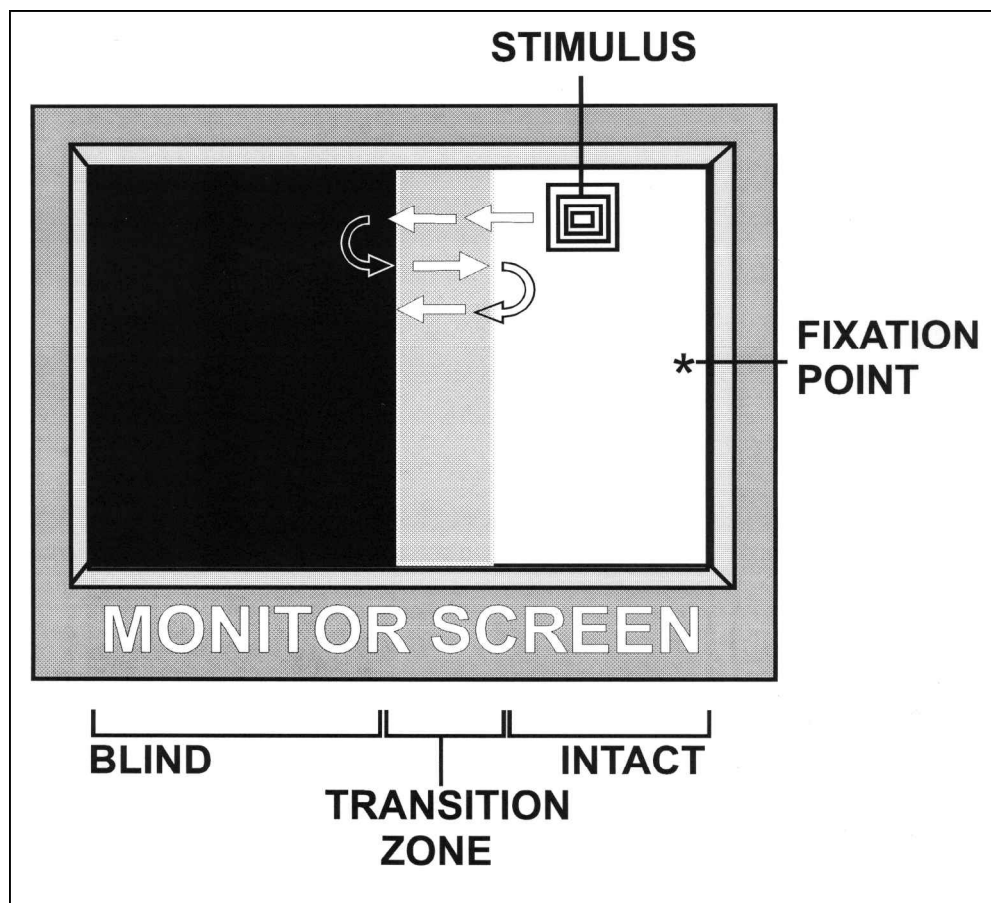
	<i>Experimental Group (n = 19)</i>	<i>Placebo Group (n = 13)</i>
Sex	58% male, 42% female	69% male, 31% female
Age	49.5 ± 3.2 years	53.3 ± 4.4 years
Years since lesion	8.1 ± 2.7 years	5.4 ± 1.4 years
Cause of damage	26.3% vascular, 52.6% trauma, 21.1% inflammation + other	30.1% vascular, 23.1% trauma, 46.8% inflammation + other
Visual field defect	52.6% homonymous, 47.4% heteronymous	38.5% homonymous, 61.5% heteronymous

Kasten & Sabel, 1995; Kasten, Strasburger, & Sabel, 1997a; Kasten, Schmielau, Behrens-Baumann, Wuest, & Sabel, 1997b; Kasten et al., 1998a; Kasten, Wuest, & Sabel, 1998b; Kasten et al., 1998c; Kasten et al., 1999; Kasten, Gothe, Bunzenthal, & Sabel, 1999a; Kasten, 1999b). Briefly, these computer-based programs allow the assessment of visual field size with much higher spatial resolution than commercially available perimeter and, thus, were termed high-resolution perimetry (HRP) (Kasten et al., 1998c). Vision was investigated by tests for detection of stimuli, shape recognition, and color discrimination. Patients were instructed to look at a fixation point at the center of the monitor throughout the examination and to respond to the visual stimulus by pressing a key on the computer keyboard within about 750 msec. In order to maximize the visual field area tested by our programs, we chose a distance of 30 cm from the computer screen so that perimetric data could be collected in an area of 21.5° vertical and 27° horizontal eccentricity from a central fixation point or, using fixation points at the borders of the screen, up to 43.0° vertical and 54.0° horizontal eccentricity. The first 20 stimuli of each session were used to get the patients accustomed to the program; data from these initial trials were not included in subsequent analyses. Each test lasted 15–20 min, depending on the size of the blind

area. For the baseline and the final outcome investigations, high-resolution computer campimetry of stimulus detection, form and color recognition were repeated five times each. The complete baseline examination therefore encompassed a total of about 10 hr (including computer perimetry, TAP perimetry, attention tests, and rest periods between the separate examinations). Testing was conducted in five independent sessions of about 2 hr each on five different days.

A complete HRP consisted of three programs: “PeriMa” measured the patients’ responses to small, stationary white dots that were presented for about 150 msec in a randomized sequence at 500 different positions in a 25 × 20 grid on a dark monitor screen (stimulus size: 0.15°, stimulus luminance: 95 cd/m², background luminance: < 1 cd/m²). “PeriForm” tested the ability to recognize forms, e.g., lines of different orientation or letters. In this study, we used letter stimuli “A,” “B,” “C,” and “D,” which were also presented for about 150 msec each at 250 randomly chosen positions on a black background (stimulus size: 2°, luminance: 50 cd/m², background: < 1 cd/m²). Upon identifying the target, the patient pressed one of four marked keys on the keyboard. Color recognition was tested using the program “PeriColor.” The subject’s task was to differentiate between three colored squares (red, green, blue)

Figure 3. The *Visure* program was used to stimulate the transition zone between the intact and the blind visual field. A large white square, which rhythmically changed its size, moved from the intact visual field into the borderline area. The patient is instructed to press a key upon detection of the stimulus. The square then moves further into the direction of the blind area. If the patient is unable to see the stimulus at a given position, it retracts back into the intact area and the procedure is repeated.



and a gray square, presented at 250 positions in randomized order on a black background with a presentation time of about 150 msec each (stimulus size: 2.5° , luminances: 25–95 cd/m^2 , background: $< 1 \text{ cd}/\text{m}^2$). To control for the quality of fixation throughout the measurements, an indirect monitoring method was used. The fixation point (a star of 4 mm diameter) changed its color in random intervals from bright green ($95 \text{ cd}/\text{m}^2$) to bright yellow ($100 \text{ cd}/\text{m}^2$) for about 150 msec. The number of changes and the time between changes of the color of the fixation point were randomized. The patient had to press a key whenever the change of color was detected. These changes could only be recognized when the patient looked directly at the fixation point. Only patients with normal fixation ability were included in the present trial. For a detailed description of these programs and normative data, see Kasten et al. (1997a, 1999a,b).

Training

After baseline measurements of the visual field defect, each patient assigned to the experimental group received a disk with the training software adapted to her/his specific deficit (Visure, SeeTrain), while each subject in the placebo group received foveal fixation training (FixTrain). Patients were instructed to train

for 1 hr each day in a darkened room at home for a minimum of 150 hr within 6 months. The results of every session were saved on disk for subsequent analysis.

Whenever the patient had reached a predetermined level of performance, the difficulty of the program was adjusted to the next level (e.g., smaller size of stimuli, decreased contrast of stimuli). Compliance checks and adaptations of training difficulty, as well as control examinations with HRP were carried out monthly. The rationale for using an individually suited procedure was to increase the therapeutic benefit and compliance by avoiding nonchallenging or overchallenging training levels.

Restitution Training

The Visure program (see Figure 3) was developed to stimulate systematically the border between intact and deficient zones of the visual field. Here, a large white square that rhythmically changed its size (to maximally activate residual functions) moved from the intact visual field towards the border area. The patient was instructed to press a key as long as she/he was able to perceive the stimulus. The square then moved further into the direction of the blind area. If the patient was unable to see the stimulus at this position, the stimulus

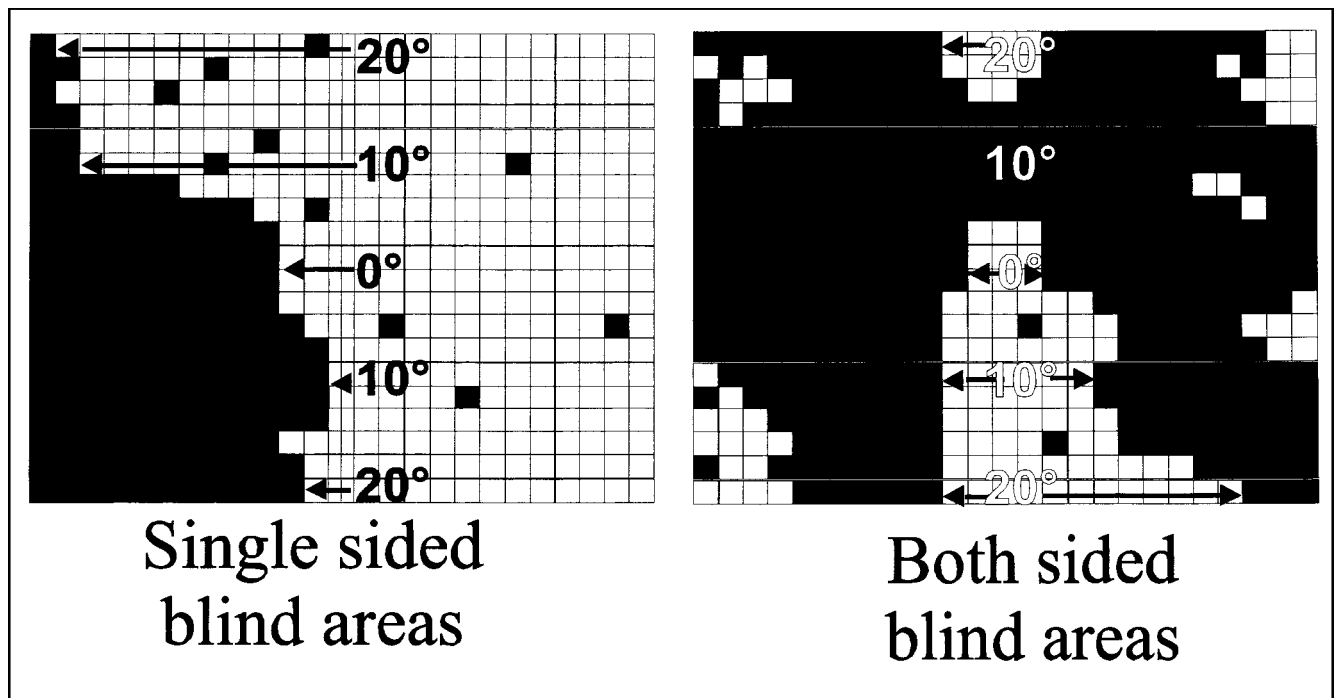


Figure 4. Typical results from high-resolution campimetry of two patients. Here, the fixation point is located in the visual of the center field (0°). Black squares indicate undetected stimuli positions and white squares intact visual areas. The border between intact and blind was quantified by measuring the horizontal distance from the vertical meridian at the positions of upper 20° , upper 10° , 0° , lower 10° , and lower 20° of visual angle. In patients suffering from unilateral visual field defects (left panel), these measurements only refer to the defective half-field. In patients with visual field defects in both hemispheres (right panel), we calculated the mean distance between the vertical meridian and the left and right visual field border. The position of the borderline was defined as that point with a minimum of two undetected stimulus positions in order. For baseline and final outcome results, these measurements were repeated five times and the average was counted.

automatically changed the direction of its movement and retracted back into the intact area. The procedure was repeated for each horizontal position at the visual field border, so that the transition zone was stimulated systematically. In contrast, stimuli presented with the program SeeTrain were stationary. Patients had to detect the stimulus as quickly as possible and press a response key while the stimulus increased in size or in brightness (from dark gray to white). Task difficulty could be adjusted by adapting stimulus size or brightness to the patient's individual level of performance.

Placebo Training

The placebo condition consisted of a fixation training program (FixTrain). The task required the patient to make eye movements to stimuli near the foveal region that changed their form or position at random intervals. While the two restitution training programs required stable fixation throughout the session so that the transition zone could be stimulated efficiently, in the placebo training FixTrain, only foveal regions were stimulated since the patient had to look directly at the stimuli in order to perform the task.

Investigation of the Visual Field Border

The position of the visual field border between the deficient and the intact region was determined by measuring the horizontal distance from the vertical meridian at the positions of upper 20°, upper 10°, 0° (center), lower 10°, and lower 20° of visual angle, respectively (see Figure 4). In patients suffering from unilateral visual field defects, the data only refer to the defective half-field. In patients with visual field defects in both hemispheres (i.e., most patients with lesion of the optic nerve), we calculated the mean distance between the vertical meridian and the left and right visual field border. Many patients had no clear border between the intact and the defective visual field, but rather displayed a large transition zone and scattered deficits. The visual field border was defined by the distance between the vertical meridian and the first stimulus location in which a minimum of two subsequent undetected stimulus events occurred.

Statistics

Statistical analyses were performed with the STATISTICA program (StatSoft, Tulsa, OK, 1995). Level of significance was defined as $p < .05$, all results are referred to as means \pm standard errors of the mean.

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