



## Neglect and Hemianopia Superimposed

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### ABSTRACT

In patients with posterior-parietal brain damage it is often difficult to decide whether left-sided omissions in perimetry are due to primary visual loss or due to visual neglect. We investigated 11 patients with combined neglect/hemianopia and 11 patients with pure hemianopia using a visual search task with single or double stimulation conditions. The second stimulus was either the fixation point itself (like in perimetry) or a distractor appearing in the hemifield opposite to the target. The fixation point did not worsen left-sided perception, but its disappearance led to a bias of exploration towards the right side in neglect patients but not in pure hemianopics. A distractor in the intact hemifield worsened the performance to left-sided stimuli, that is, neglect patients behaved as if they were completely hemianopic, even in intact parts of the visual field (VF). Three of the neglect patients showed unconscious processing of the distractor in the left VF, suggesting that the visual field defect was produced by neglect mechanisms rather than primary visual loss. This visual search paradigm appears to be helpful in understanding of the nature of hemianopia versus neglect deficits in individual patients.

### INTRODUCTION

Patients with right hemispheric damage often show hemispatial neglect, that is, they unintentionally orient attention to the ipsilesional side of space and become unaware of events on the left. Among the multiple deficits of perception and exploratory behavior that constitute the neglect syndrome, extinction is often taken as the cardinal sign of attentional deficits (Bisiach, 1991; Driver, Mattingley, Rorden, & Davis, 1997; Rafal, 1994; Vuilleumier & Rafal, 2000). Visual extinction describes the phenomenon that, during simultaneous stimulation in both hemifields, contralesional stimuli are extinguished from awareness, but they are reported correctly when presented alone. Contralateral extinction and neglect are

distinct phenomena and whether they share the same common mechanisms has been questioned because there are patients who show neglect but no extinction (Barbieri & De Renzi, 1989; Olivieri et al., 1999). Both, neglect and extinction, are more frequent after right hemispheric damage (Barbieri & De Renzi, 1989; Vuilleumier & Rafal, 2000), but they appear to have somewhat different neuroanatomical correlates (Vallar, Rusconi, Bignamini, Geminiani, & Perani, 1994). Recent studies (Farah, Monheit, & Wallace, 1991; Marzi et al., 1996; Olivieri et al., 1999) suggest that extinction might result from a sensory imbalance due to a breakdown of hemispheric rivalry (Kinsbourne, 1977, 1993). It is thought that the cortical activation by the contralesional stimulus is weakened by backward projections from

(lesioned) parietal areas to striate cortex (Graves & Jones, 1992). Because of this lowering of the activity in striate and extrastriate areas in the lesioned hemisphere the stimulus might, in consequence, not be perceived under competing stimulus conditions. It is assumed that an intact geniculo-striate pathway (i.e., the primary perceptual function) and intact inferior occipital-temporal areas (i.e., higher-order visual recognition) are sufficient for conscious vision. Stimuli can be perceived and recognized, and thus conventional perimetry is normal (Graves & Jones, 1992). In the case of neglect, however, these brain areas may not be fully sufficient: although lesions are located outside the primary visual areas, particularly in the right inferior parietal lobe, neglect patients often appear to have perceptual deficits when their visual field is tested.

Walker, Findlay, Young, and Welch (1991), for example, described a patient who seemingly showed a visual field loss in a perimetric test, but after removal of the fixation point shortly before the test stimulus appeared, the patient was able to detect leftward stimuli. Walker and colleagues concluded that a homonymous hemianopia may be only apparent but not real in the perimetry because the fixation point induces extinction of leftward stimuli.

Kooistra and Heilman (1989) also described a neglect patient who appeared to have a left hemianopia, but when the patient moved her eyes towards the right hemispace (i.e., body axis was moved leftwards), stimulus detection in the contralesional (left) visual field improved. This was taken to suggest that the apparent field defect in this patient was caused by hemispatial inattention rather than by a functional loss of the perceptual system.

Kinsbourne postulated an attentional gradient in neglect patients with the deficit particularly affecting the leftmost of two stimuli. This is supported by studies reporting a rightward distortion of the egocentric spatial reference frame in neglect patients (Jeannerod & Biguer, 1987; Karnath, 1994, 1997).

It is possible that a posterior parietal lesion encloses parts of the optic radiation, leading to a combined disorder of hemianopia and visual neglect (Karnath, 2001; Karnath, Ferber, &

Himmelbach, 2001). On the other hand apparent visual field defects in neglect patients may also be caused, first, by limited attentional capacities under conditions of stimulus competition (i.e., the fixation point constitutes a competing stimulus), and second, by a rightward distortion of the spatial attentional egocentric reference frame.

Thus, a common difficulty of many studies with neglect patients ignoring contralesional visual stimuli is the inability of the experimenter to correctly evaluate whether the patient has also a superimposed hemianopia. Because neglect and hemianopia represent functionally unrelated disorders – they differ in lesion localization, exploratory behavior and prognosis (Halligan, 1999; Halligan, Marshall, & Wade, 1990) – differential diagnosis is essential. To clarify this, the following hypotheses were now tested: First, in patients with neglect and additional hemianopia, the fixation point in a perimetric test may induce a condition of double simultaneous stimulation (i.e., stimulus competition) that leads to extinction of contralesional stimuli. Here, the presence of a fixation point would be expected to impair the performance (e.g., detection rate, reaction time) in the damaged hemifield. Because the extinguished stimulus is found to be unconsciously processed in patients with intact visual fields (Berti et al., 1992; Driver & Mattingley, 1998; Marzi et al., 1996; Volpe, Ledoux, & Gazzaniga, 1979; Vuilleumier & Rafal, 2000; Vuilleumier et al., 2001) an effect of the distractor in the defect hemifield would indicate early visual processing in striate and extrastriate areas (Rees et al., 2000). Second, should the omissions in the contralesional hemifield be caused by a distorted spatial reference frame, one would expect detection performance and reaction times to depend on stimulus eccentricity. Third, in neglect patients with superimposed hemianopia neither stimulus competition (e.g., presence of a fixation point or an additional competing stimulus) nor eccentricity should play a role.

## METHODS

### Patients

Patients were recruited from stroke units of cooperating hospitals in Berlin and Magdeburg. Forty-three patients

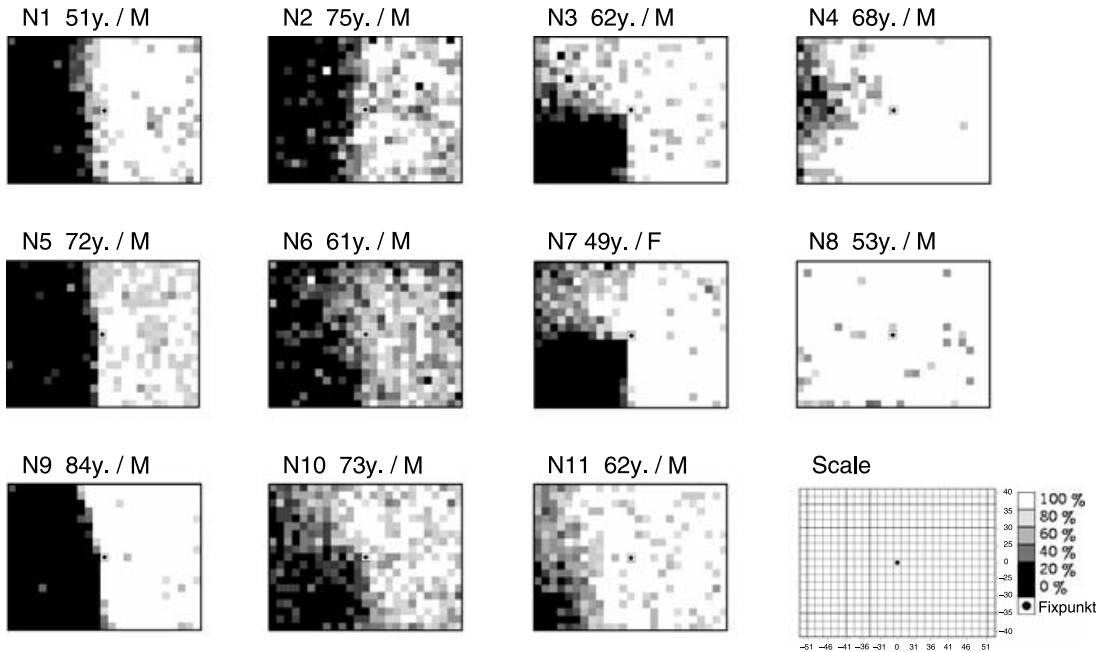


Fig. 1. High-resolution perimetry (HRP) of the neglect patients. HRP measurements of each patient were superimposed, with white and black areas representing intact and blind regions, respectively, and gray areas regions in which stimulus detection is unreliable. Each graph shows patient ID, age and sex. Size of visual field displayed in degrees of visual angle ( $^{\circ}$ ), that is,  $52^{\circ}$  ( $\pm 26^{\circ}$ ) horizontally and  $40^{\circ}$  ( $\pm 20^{\circ}$ ) vertically.

were screened; 22 patients were included in the study who fulfilled the criteria of having a homonymous hemianopia or visual neglect, with a lesion age of at least 3 months. The lesion location was occipital and/or parietal. Patients with ophthalmic diseases were excluded. Informed consent was obtained. We investigated two experimental groups of patients. One group consisted of 11 patients with a diagnosis of neglect (mean age  $64 \pm 11$  years). Ten of these exhibited anopic areas in their left, contralesional hemifield, ranging from complete hemianopia to paracentral quadrantanopia (see Fig. 1). The other group consisted of patients with pure homonymous hemianopia, six left- and five right-sided ( $n = 11$ , mean age  $50 \pm 13$  years) and no neglect (see Fig. 2).

The two groups differed significantly in age ( $p < .01$ ; Mann-Whitney  $U$  test), the neglect patients being older on average. Except for two cases in the hemianopic group, all patients were right handed. Age of lesion (AL) in the hemianopic group ranged from 3 months to 18 years (mean:  $4\frac{1}{3}$  years) and in the neglect group from 3 months to  $3\frac{1}{2}$  years (mean:  $1\frac{1}{2}$  years;  $p = .076$ ; Mann-Whitney  $U$  test). The large range in the hemianopic group is due to 2 patients with a lesion age of 6 and 18 years,

respectively. Demographic and clinical patient data are shown in Table 1.

### Lesion Characteristics

Radiological brain scans showed cortical lesions (Table 2), predominantly involving occipital areas in the hemianopic group (8 of 11: 8 occipital, 1 parieto-occipital, 1 temporo-parietal, 1 temporo-occipital) and parietal areas in the neglect group (2 parietal, 4 parieto-occipital, 1 temporal, 2 temporo-parietal, 2 temporo-parieto-occipital). Eleven patients (hemianopic: 5, neglect: 6) had also subcortical lesions, involving, in the neglect group, in three cases the basal ganglia and in one case the thalamus. The two groups differed significantly with regard to the location of the cortical lesions ( $\chi^2 = 16.13$ ;  $p < .002$ ; Pearson Chi Square), but not with regard to the presence of subcortical lesions ( $\chi^2 = 5.4$ ;  $p = .14$ ; Pearson Chi Square). Overall, most patients presented cerebro-vascular etiology (neglect group: 10 infarction, 1 resection of a tumor; pure hemianopic group: 7 infarction, 1 resection of a tumor, 2 aneurism bleeding and operation, 1 trauma from car accident). Etiology was not significantly different between the two groups ( $\chi^2 = 3.53$ ;  $p = .317$ ; Pearson Chi Square).

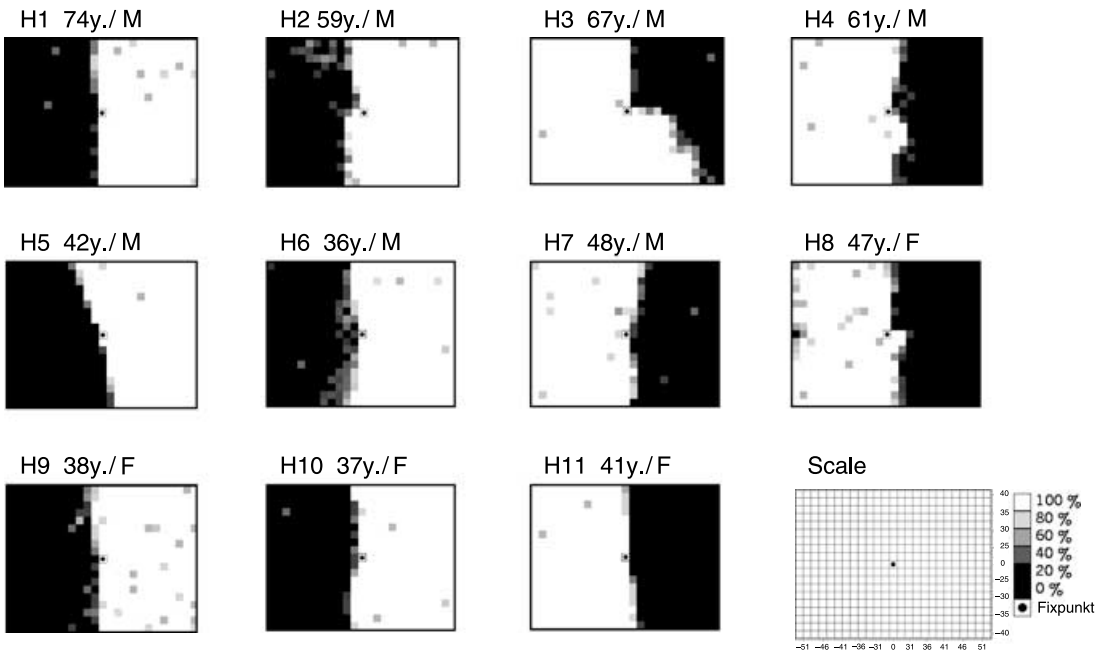


Fig. 2. High resolution perimetry (HRP) of the hemianopic patients. Parameters same as in Figure 1.

Table 1. Demographic and Clinical Data of the Subject Groups.

	Age (years)	AL (months)	VF %	Fix %	Diagnosis of neglect (n)			
					Severe	Mild	Residual	None
Hemianopia	50 ± 13	52 ± 64	53 ± 4	98.7 ± 0.9	0	0	0	11
Neglect	64 ± 11	18 ± 11	63 ± 17	87.7 ± 18.5	4	4	3	0

Note. AL = age of lesion, VF % = percent of intact visual field, Fix % = fixation ability, that is, percent correct responses, diagnosis of neglect (n) = number of occurrences.

**Diagnosis of Neglect**

Testing for inclusion into the neglect group, 8 patients showed symptoms of hemispatial neglect in the Behavioral Inattention Test (BIT; Wilson, Cockburn, & Halligan, 1987; Table 3a), which includes tasks of line bisection, cancellation, copying, and free drawing. To catch less severe symptoms of neglect we also used a cancellation task administered under speed conditions (Alters-Konzentrationsstest, AKT; Gatterer, 1990) that included one familiarization and three test forms. Three patients presenting severe neglect immediately after infarction showed, at the time of testing (3, 8, and 41 months post lesion), neglect symptoms only under speed conditions (ratio of left- to right-sided misses for each patient: 14/2; 7/1; 10/4, respectively); additionally, these patients, or their relatives, reported having

certain difficulties in every-day activities that led to the assumption of residual neglect (bumping into an opened door on the person’s left, choosing the right one of two seats; the tendency to spontaneously turn rightward after leaving the house, etc.). The neglect patients’ mean BIT score was 126 ± 15 (SD) (n = 11). In contrast, all patients of the hemianopic group reached high scores in the BIT test (143 ± 2), which corresponds to the absence of neglect (maximum BIT score: 146). The score difference between the groups was highly significant (p < .0001; Mann-Whitney U test). In the AKT, the groups were significantly different in the contra- to ipsilesional ratio of misses, with the neglect group showing significantly more contralesional misses (p < .001; Mann-Whitney U test).

Table 2. Clinical Patient Characteristics (H = Hemianopic Group; N = Neglect Group).

Case	Age (years)	Sex	AL (months)	VFD	Neglect	Extinction	Lesion side	Lesion site	SC
N1	51	M	6	+	Sev.		R	PO	+
N2	75	M	3	+	Sev.		R	TPO	+
N3	62	M	8	+	Res.	+	R	TP	+
N4	68	M	17	+	Mild	+	R	T	+
N5	72	M	3	+	Res.		R	PO	-
N6	61	M	11	+	Sev.		R	P	-
N7	49	F	41	+	Res.	(+)	R	TP	-
N8	53	M	18	-	Mild	+	R	P	+
N9	84	M	9	+	Mild		R	TPO	-
N10	73	M	20	+	Sev.	+	R	PO	+
N11	62	M	4	+	Mild	+	R	PO	-
H1	74	M	3	+	-		R	O	-
H2	59	M	24	+	-		R	O	+
H3	67	M	24	+	-		L	O	-
H4	61	M	3	+	-		L	O	-
H5	42	M	216	+	-		R	TO	-
H6	36	M	8	+	-		R	TP	+
H7	48	M	18	+	-		L	PO	+
H8	47	F	92	+	-		L	O	+
H9	38	F	116	+	-		R	O	-
H10	37	F	35	+	-		R	O	+
H11	41	F	34	+	-		L	O	-

Note. (AL = Age of Lesion; VFD = Presence of a Visual Field Defect in Perimetry; M = Male; F = Female; Sev. = Severe; Mild = Mild; Res. = Residual; R = Right; L = Left; Lesion Site Abbreviations: T = Temporal; P = Parietal; O = Occipital; SC = Subcortical).

Confrontation testing was used to examine visual extinction, that is, the patients had to indicate the experimenter's movement of one versus both hands, positioned in the left and right visual field, respectively, while steadily fixating the experimenters' face. The test is meaningfully only applied for those patients who react to single stimuli, which was the case for 6 of the neglect patients. These patients, on average, showed visual extinction of  $69 \pm 39\%$  ( $Md = 85\%$  range from 5 to 100%) of the left stimuli under double stimulation, while detecting 100% when stimuli were presented singly.

### Perimetry

All patients underwent standard perimetric testing on a Tuebinger Automated Perimeter (TAP-2000). Subjects fixated a point in the center of the sphere and reacted to the appearance of a circular disk stimulus appearing in the visual field. For a spatially more detailed assessment of the central visual field, qualitative high-resolution perimetry (HRP) was also applied in repeated sessions. Since all visual field defects were approximately homonymous in the TAP measurements, HRP measurements were carried out binocularly. The

qualitative high-resolution perimetry was performed with a computerized diagnostic system (manufactured by NovaVision, Magdeburg) which tests detection of small, bright, supra-threshold light spots ( $100 \text{ cd/m}^2$ , 0.3 cm diameter) at 474 positions in the central visual field. Fixation was controlled by a brief change of the fixation point's color (from green:  $120 \text{ cd/m}^2$ , to yellow:  $120 \text{ cd/m}^2$ , 150 ms, 0.3 cm diameter) to which the subject was instructed to respond by pressing a key on the computer keyboard. The program is a successor of the PeriMA program described by Kasten, Strasburger, and Sabel (1997) and is similar in its stimulus characteristics and approach. In a previous evaluation of HRP data, Kasten, Gothe, Bunzenthal, and Sabel (1999) showed that visual field data measured by TAP and by HRP to be highly compatible ( $r = .78$ ;  $p < .05$ ). HRP measurements are shown to be highly stable enabling repeated testing (Kasten, Müller-Oehring, & Sabel, 2001). Subjects viewed stimuli on a 17-in. computer monitor at a viewing distance of 30 cm. Using a forehead-chin rest to minimize head movements during testing, the resulting visual angle was  $\pm 27^\circ$  horizontally and  $\pm 20^\circ$  vertically. We recorded stimulus detection, false positives and the number of correctly

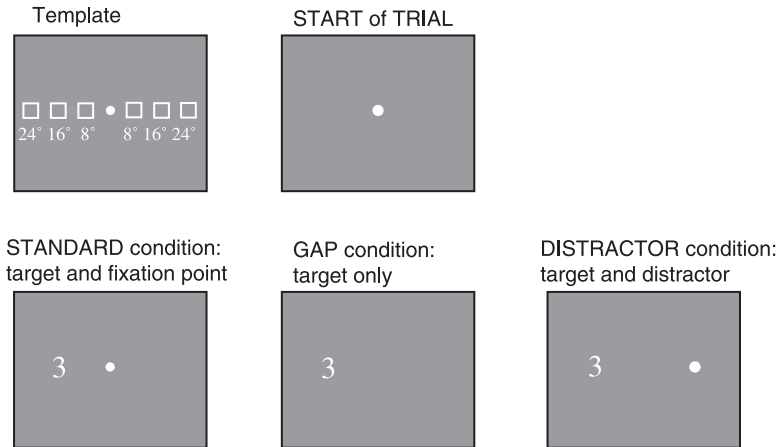


Fig. 3. The three stimulus conditions of the visual search task: (1) STANDARD condition: both the fixation point and target stimulus (a digit) are presented simultaneously; (2) GAP condition: the fixation point disappears 200 ms before onset of the target; (3) DISTRACTOR condition: as in Condition 2, the fixation point disappears, but a second stimulus (a distractor) appears simultaneously with the digit, at the same horizontal eccentricity but contralateral to the digit in a mirror symmetric position.

detected fixation controls. HRP measurements of each patient were superimposed (see Figs. 1 and 2). White and black areas thus represent intact and blind regions, respectively, and gray areas show regions in which stimulus detection is unreliable, that is, in which a stimulus is detected unreliably, either due to residual visual or to limited attentional capacities (Kasten, Wüst, & Sabel, 1998).

### Experimental Paradigm

To examine whether the fixation point constitutes a condition of double simultaneous stimulation leading to contralesional extinction, we varied the presence of the fixation point. Since neglect patients cannot hold steady fixation when the fixation point disappears, we created a visual search design. For better comparison of data, the search test was implemented within the program for HRP measurements, with the fixation point and test conditions being identical (17 in. monitor, 30 cm viewing distance, forehead-chin rest, same color and luminance of stimuli and same background, room illumination). The task was to focus on the fixation point. In addition to the fixation control by a brief color change, the experimenter observed the subject's eyes through a mirror. A tone indicated the onset of the target stimulus, which was one of the three digits "2," "3" or "8." Stimuli were presented at one of six horizontal locations within the central visual field (at  $\pm 8^\circ$ ,  $\pm 16^\circ$  and  $\pm 24^\circ$  eccentricity). The task was to search for the digit and to respond to it by pressing one out of three keys as quickly as possible. A time-out was set at 30 s; the next trial started either after the patient's reaction or after the time-out, with an inter-trial-interval of 2.5–4.5 s.

In each test session, three stimulus configurations were presented in a pseudo random order (Fig. 3): (1) both the fixation point and target stimulus (STANDARD condition); (2) the fixation point disappearing 200 ms before target onset (GAP condition); (3) the fixation point disappearing (like in condition 2) but a second, distractor stimulus (a point) appearing simultaneously with stimulus onset, at the same eccentricity ( $8^\circ$ ,  $16^\circ$ ,  $24^\circ$ ) but contralateral to the target (DISTRACTOR condition). For example, under double stimulus conditions the digit was at  $8^\circ$  in the right visual field and the competing distractor was at  $8^\circ$  in the left visual field and so on. Measurements were repeated three times to control for reliability. Mean search reaction times were computed for the stimulus locations in each patient.

### Statistical Data Analysis

Statistical analysis was carried out with the SPSS package (Standard Version 8.0, 1997). The Mann-Whitney *U* test was used for group comparison and the Wilcoxon test was employed for the comparison of conditions. Nonparametric correlation, that is, Spearman's rho, was applied to test the relationship between two variables. Significance was tested at the 5% level.

### RESULTS

At first we considered whether the performance in the perimetric task and in the experimental paradigm are correlated. As expected, in patients with neglect, stimulus detection in high resolution

perimetry (HRP) was highly correlated with stimulus detection time in the visual search paradigm (OVERLAP condition: with the fixation point present) in the contralesional hemifield ( $r = -.80$ ), but not with performance ipsilesionally (Table 3). In contrast, in hemianopic patients, the two tasks did not correlate significantly. Thus, contralesional search performance in the visual search task and detection performance in the contralesional perimetric visual field (both with fixation point present) are closely related in neglect patients and may be governed by a common functional deficit.

Analysis of the search times in the STANDARD condition (with fixation point present) revealed overall prolonged responses to stimuli in both hemifields in neglect group compared to the pure-hemianopic group (intact hemifield: 1131 vs. 875 ms;  $p < .001$ ; defective hemifield: 2591 vs. 1269 ms;  $p < .001$ ). As expected, all 22 patients showed significantly longer search times in the defective than in the intact hemifield. However, this difference was much more pronounced in the neglect patients showing a difference in reaction time between contra- and the ipsilesional hemifield of 1167 ms, whereas in the pure-hemianopic group it was only 366 ms ( $p < .02$ ). We studied the influence of visual eccentricity within the contralesional hemifield and found, in accordance to other studies (Behrmann, Watt, Black, & Barton, 1997; Karnath, Niemeier, & Dichgans, 1998; Kinsbourne, 1993), the largest difference in visual search time between hemianopic and neglect patients at the outermost position ( $p < .0001$ ; group difference at  $24^\circ$ : 2053 ms), followed by  $16^\circ$  ( $p < .0001$ ; difference: 1000 ms) and  $8^\circ$  ( $p < .001$ ; difference: 593 ms). In the ipsilesional hemifield the difference between the groups was smaller but still highly significant and independent of eccentricity ( $8^\circ$ : 318 ms;  $16^\circ$ : 208 ms;  $24^\circ$ : 305 ms; for all  $p < .0001$ ) (Fig. 4).

### Stimulus Competition Between a Target Stimulus and the Fixation Point

We investigated also the question whether the fixation point, as a competing stimulus, might inhibit the reaction to contralesional stimuli in neglect patients in comparison to pure hemianopics. In neglect patients the disappearance of the

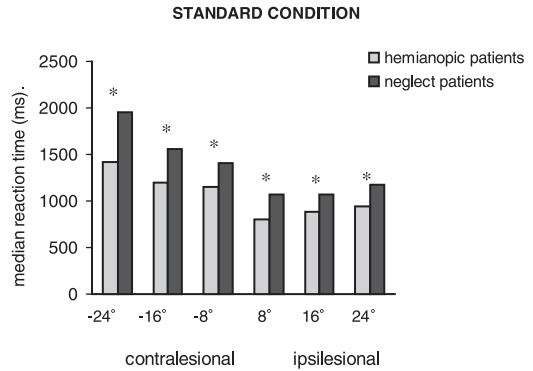


Fig. 4. Visual search time in the STANDARD condition (fixation point and target stimulus simultaneously present) at six horizontal eccentricities in the patient groups. Group median values are reported.

fixation point (GAP condition) had no effect whatsoever, that is, visual search times did not change in either hemifield. In the hemianopic group, search times were significantly reduced in the defective hemifield ( $p < .003$ ) compared to the STANDARD condition, but this was not the case in the intact hemifield. Moreover, we found no significant correlation between the influence of the fixation point in the visual search paradigm (i.e., the difference in reaction time between the conditions with versus without fixation point) and the percentage of detected stimuli in HRP measurements in neither group (Table 3). Thus, any benefit or cost from the disappearance of the fixation point is independent of the visual field defect.

Since we found that visual search times were dependent on eccentricity (Fig. 4), we asked whether the disappearance of the fixation point has different effects on different visual field locations. In hemianopics, we observed a decrease of reaction times at all three contralesional positions ( $8^\circ$ :  $-88$  ms,  $16^\circ$ :  $-81$  ms,  $24^\circ$ :  $-88$  ms; for all:  $p < .01$ ), whereas in the intact hemifield it had an opposite effect. Here, slightly prolonged reaction times were noted at the outermost position ( $24^\circ$ ) ( $+42$  ms,  $p < .01$ ). In contrast, in the neglect group, removal of the fixation point tended to slightly reduce reaction times at  $24^\circ$  ipsilesionally (94 ms,  $p = .1$ ). Between-group comparison of these difference values (Fig. 5) yielded significantly different

Table 3. Correlation Coefficient of HRP Data (Percent of Stimuli Detected) and Visual Search Performance (Visual Search Time Until Stimulus Detection) in Patients with Neglect and with Pure Hemianopia.

	Visual field		
	Total	Contralesional	Ipsilesional
<i>(a) Correlation of HRP with search time (STANDARD condition)</i>			
Neglect ( $n = 11$ )	-0.80**	-0.86**	-0.32
Hemianopia ( $n = 11$ )	0.21	0.14	0.41
<i>(b) Correlation of HRP with the influence of fixation point (difference values of STANDARD-GAP condition)</i>			
Neglect ( $n = 11$ )	-0.32	0.02	0.05
Hemianopia ( $n = 11$ )	-0.29	-0.46	0.00

\*\* $p < .001$ .

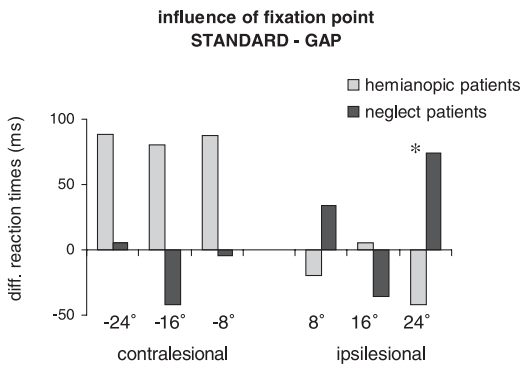


Fig. 5. Difference values of STANDARD-GAP, that is, influence of the fixation point, at six horizontal eccentricities in the two patient groups.

effects only at this outermost position (24°) of the intact hemifield ( $p < .01$ ).

The mean gain in reaction time with removal of the fixation point is rather small and the question therefore arises whether all patients show that effect. We compared how many patients in each group reacted with an increase versus a decrease in visual search time: At the outermost position (24°) in the intact hemifield, reaction times were prolonged in 10 hemianopics whereas 9 out of 11 neglect patients exhibited faster reaction times ( $\chi^2 = 11.73$ ;  $p < .002$ ; two-sided; Pearson Chi Square).

**Stimulus Competition Between a Target and a Distracter Stimulus**

To assess the effect of possible competition among the simultaneously appearing contralateral

distracter stimulus and the ipsilateral target, we compared reaction times in the DISTRACTOR condition (i.e., double simultaneous stimulation) to those in the GAP condition (i.e., single stimulation). Stimulus competition in our paradigm takes place with the distracter being opposite to the target in either (a) the intact, ipsilesional or (b) the defect, contralesional hemifield.

**(a) Inhibition of Perceiving Contralesional Stimuli by the Ipsilesional Distractor**

The ipsilesional distractor stimulus led to a significant prolongation of visual search times to the (contralesional) target stimulus in both groups (mean = 588 ms in neglect patients:  $p < .01$ ; 324 ms in hemianopic patients:  $p < .003$ ). Longer reaction times were observed at all eccentricities in the neglect and the hemianopic patients (neglect: 24°, 16°,  $p < .04$ , and 8°,  $p < .008$ ; hemianopic: 24°, 16°, 8°,  $p < .003$ ). The prolongation was more pronounced in neglect patients ( $p < .05$ ). Three neglect patients had problems finding the stimulus at 24° visual angle within the time limit of 30 s, which causes a high variance of search times in that group (range of reaction times at 24° in the defect hemifield; neglect group: range = 19 s, 378 ms, hemianopic group: range = 311 ms).

**(b) Processing of the Contralesional Distractor**

Appearance of the (contralesional) distractor did not influence reaction time to the target in any of the three spatial locations (8°, 16°, 24°) in the ipsilesional hemifield, neither in the hemianopic



nor in the neglect group. Under detailed consideration of the visual fields of each single patient, 6 neglect patients showed areas of intact perception contralesionally in HRP (N3, N4, N7, N8, N10 and N11, see Fig. 2). Thus, in principle they should be able to perceive the distractor appearing in the contralesional hemifield. In these specific parts of the visual field the two stimuli should represent a competitive condition that would be expected to increase reaction times to the ipsilesional target stimulus. Thus, in a single case analysis of these patients' search times, we tested if the reaction times (RT) in the intact (ipsilesional) hemifield changed when a contralesional distractor was present. Processing of the contralesional distractor was measured indirectly by computing it according to the following rationale:

$$RT(\text{GAP: target ipsilesionally}) - RT(\text{DISTRACTOR: target ipsilesionally}) \neq 0.$$

That is, the reaction time to the target in the intact hemifield differs when a competing stimulus is simultaneously presented in the "defective" hemifield contralateral to the lesion. Three neglect patients (N7, N8, N10) showed processing of the contralesional distractor (N7:  $p < .01$ ; N8:  $p = .05$ ; N10:  $p < .04$ ). In the remaining 8 patients with neglect, no effect of double simultaneous stimulation was seen with the distractor appearing contralesionally. None of these patients reported

having perceived the contralesional distractor in an interview following the testing sessions. The neglect patients thus behaved as if they were completely hemianopic, although some showed intact parts of the contralesional visual field in perimetry. Thus, in neglect patients, even if they only show residual neglect, extinction of a contralesional stimulus can be achieved using a competitive stimulus design.

**Stimulus Competition and Visual Field Data**

We next studied the relationship between perimetric visual field results and the performance in competitive stimulus conditions. In particular, we were interested in the processing of the contralesional distractor. For this reason data of the visual search task and perimetry were measured at 15 locations in each hemifield, that is, at three horizontal (at 8°, 16°, 24°) times five vertical (at 0°, ±8°, ±16°) positions (see Fig. 6).

We correlated the computed difference of reaction times between the GAP and DISTRACTOR conditions (influence of the distractor, see above) with the percentage of the number of detected stimuli in the perimetric task.

In the hemianopic group, only one patient (H3, see Fig. 1) who had an incomplete right-sided hemianopia showed a significant correlation between HRP data and the processing of the

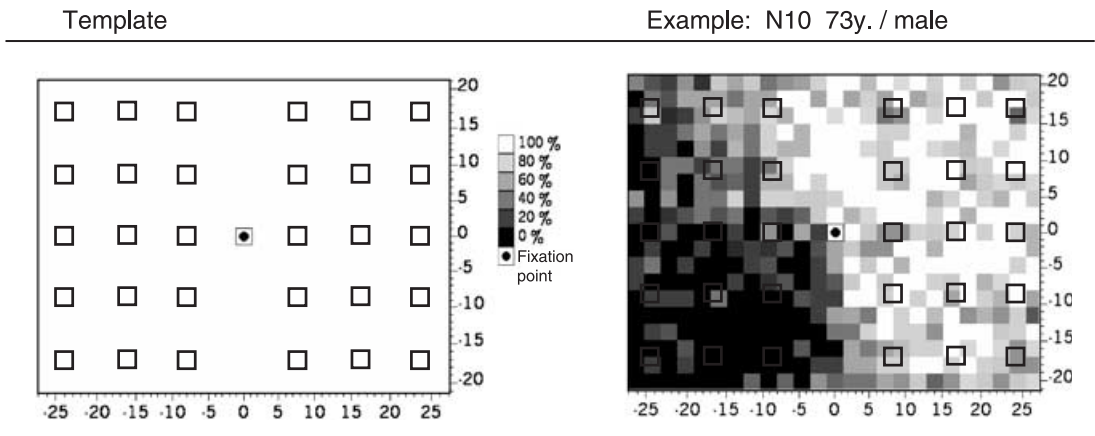


Fig. 6. Locations of the 30 visual search targets in the central visual field. Performance in these locations were used for direct comparison of the HRP and the visual search performance in each patient. Left: template; right: example with the HRP data of patient N10.

distractor at the corresponding contralesional location ( $r = .59$ ,  $p < .02$ ), that is, increased ipsilesional search times with the distractor presented contralesionally.

Of the 3 neglect patients N7, N8 and N10, who had shown processing of the contralesional distractor stimulus, the two having visual field defects (N7 and N10) showed a significant correlation between HRP data and the influence of the contralesional distractor.

In patient N7 a positive correlation was observed ( $r = .67$ ,  $p < .01$ ), that is, prolonged ipsilesional search times were associated with a higher percentage of perceived visual stimuli within the contralesional hemifield: The more stimuli the patient perceived contralesionally, the stronger the distractor competed with the target, resulting in increased reaction times. From this we propose that the visual field defect (VFD) in N7 is "real," that is, a perceptual deficit, and not produced by extinction.

The second patient (N10) showed a negative correlation between these two variables ( $r = -0.49$ ,  $p = .06$ ), that is, higher influence of the distractor was associated with *lower* HRP performance in the contralesional hemifield. A second stimulus led to an inhibition of reaction to contralesional stimuli, which is related to misses in perimetry. The apparent VFD in this patient thus seems to be a result of this inhibition process, that is, of visual extinction under competitive stimulation.

### Stimulus Eccentricity and Visual Field Data

In HRP, single-case analysis showed a pronounced correlation between the percentage of detected stimuli and stimulus eccentricity in the contralesional hemifield in 3 neglect patients (N1:  $r = -.73$ ,  $p < .002$ ; N4:  $r = -.66$ ,  $p < .007$ ; N11:  $r = -.70$ ,  $p < .004$ ) but in none of the hemianopic patients. Thus, in 3 neglect patients (27%) stimulus detection in HRP (i.e., data of the contralesional visual field) appears to depend on eccentricity.

## DISCUSSION

Most of our patients with chronic neglect syndrome (10 out of 11) show also visual field defects

in perimetric testing. Karnath and colleagues (Karnath & Ferber, 1999; Karnath et al., 1998) suggest that neglect results from an ipsilesional rotation of the egocentric spatial-reference system. Under this hypothesis, parts of the right visual field in perimetry will be located within the left hemispace relative to an internal frame of reference rotated to the right. Because of this gradient of biased hemispacial attention from the center of the reference frame toward its periphery in neglect patients one would then expect stimulus detection in the contralesional field to decrease with increasing eccentricity of the stimulus. In contrast to hemianopic patients, where no such correlation was found, in 3 out of 11 neglect patients the detection of stimuli in the contralesional hemifield depended upon eccentricity. This suggests an influence of hemispacial inattention rather than a primary visual field loss on stimulus detection (Kooistra & Heilman, 1989).

We further found a high correlation between performance in perimetry and in visual search in the STANDARD condition for the contralesional hemifield in neglect patients. There was little or no correlation for the hemianopics. Although perimetry aims at measuring deficits due to damage of the visual system, it poses high demands on the attentional capability of the patient. A deficit in the latter, especially in the case of hemispacial inattention, may result in deficient performance in a perimetric test, since attention and perception are closely interrelated in early stages of information processing, taking place before the initiation of an eye movement (Posner, Walker, Friedrich, & Rafal, 1987).

### Visual Search and Compensation Strategies

In the STANDARD condition of the visual search task, that is, with the fixation point present, both patient groups showed increased reaction times to contralesional in comparison with ipsilesional stimuli. This side difference was more pronounced in neglect patients. Since the first studies of Poppelreuter (1917) it is well known that directly after the lesion hemianopic patients exert few eye movements into the blind area (Chedru, Leblanc, & Lhermitte, 1973; Meienberg, Zangemeister, Rosenberg, Hoyt, &

Stark, 1981; Zangemeister, Meienberg, Stark, & Hoyt, 1982), but soon adapt to the new situation and learn to compensate for the visual field loss by eye movements (Grüsser & Landis, 1991). Such an adaptation is not observed in neglect patients. Spontaneous eye movements when scanning a visual scene are mainly within the ipsilesional hemifield (Ishiai, Furukawa, & Tsukagoshi, 1989; Jeannerod, 1986). Even with our paradigm directing fixation back to the center before each trial, our results confirm that neglect patients have a deficit to compensate their loss with eye movements compared to hemianopic patients.

In the STANDARD condition of the visual search task, we found reaction times to be different between neglect and hemianopic patients, again corresponding to a right-left gradient of hemispatial attention (Behrmann, Watt, Black, & Barton, 1997; Karnath & Ferber, 1999; Kinsbourne, 1993). The two groups differ the most at the outermost position in the contralesional hemifield, the difference decreases towards the center and in the intact hemifield it was no longer dependent on eccentricity. Removal of the fixation point led to a benefit in reaction time in neglect patients (at 24° eccentricity) in the intact hemifield while hemianopics showed significant costs at this location, indicating an opposite shift of attention in the two groups, ipsilesional in neglect patients and contralesional in hemianopic patients. When patients with neglect are not forced to attend to a fixation point, their attention shifts to the right, so that retinal axis and body-centered reference axis diverge. In rehabilitation, this rightward shift of the attentional focus possibly counteracts a compensation for left-sided neglect independent of an additional visual field defect.

### **Stimulus Detection, Stimulus Competition and Visual Extinction**

We had developed a computerized paradigm to test the influence of competing stimuli on stimulus detection, the competing stimulus being either a fixation point or a distractor that appeared simultaneously with the target but in the opposite hemifield. Unlike in hemianopics, neglect patients did not benefit from the fixation point's disappearance. Moreover, there was no significant

correlation between the visual field defect and the effect of the fixation point. From this we conclude that the fixation point does not compete with the target stimulus. It is also not responsible for a failure of neglect patients to detect contralesional stimuli.

Competition was observed, however, in the DISTRACTOR condition. Neglect patients showed drastically prolonged reaction times when the distractor stimulus appeared in the intact hemifield; hemianopic patients also showed significantly prolonged reaction times, though less so than neglect patients. An explanation for this extinction-like response pattern in hemianopics can be derived from cueing experiments (Posner, Walker, Friedrich, & Rafal, 1984; Posner et al., 1987): When a cue (a distractor in our paradigm) summons attention towards the ipsilesional hemifield, with the target being presented subsequently (or simultaneously in our paradigm) in the contralesional hemifield, reaction time (RT) will slow dramatically (for review see Rafal, 1999); that is, if the target appears in the blind field, double stimulation is subjectively perceived as an "invalid" cueing condition. Thus, prolonged reaction times to a contralesional target can be induced (a) by invalid cueing when there is sensory loss of vision or (b) by extinction. In case of simultaneous stimulation, neglect patients will behave as if they were hemianopic either due to a sensory deficit and/or extinction.

To disentangle hemianopia and extinction within a patient, we thus performed single case analysis on the relationship of unseen stimuli in HRP and unconscious processing of the extinguished distractor.

Visual extinction can, by definition, only occur in patients with intact striate cortex and therefore the extinguished stimulus might be processed unconsciously. Some patients in our neglect group showed intact or partly intact parts of the contralesional visual field in perimetry, and the question arises whether unconscious processing occurred in these parts of vision. Three neglect patients (N7, N8 and N10) showed significantly prolonged RT to targets in the intact hemifield when the distractor appeared in the contralesional hemifield, although it was extinguished from awareness as shown by the failure to mention the

contralesional distractor in an interview immediately after the test. Patient N8 had fully intact and N7 and N10 partly intact visual fields. One of the hemianopic patients (H3) also had an intact area in his otherwise blind field. In H3 and N7 we found a significant positive correlation between detection rate in HRP and reaction time (RT) in the DISTRACTOR condition (with the distractor at 15 different locations within the contralesional hemifield), that is, the more intact the visual fields, the more did the contralesional distractor stimulus compete with the ipsilesional target stimulus, resulting in increased RT. From this we conclude that the perimetric measurement (HRP) has validly determined the visual field defects in N7 and was not influenced by extinction. N10, in contrast, showed a negative relationship between detection rate in HRP and the influence of the distractor at the same visual field locations, that is, the fewer stimuli were perceived in HRP, the more competed the contralesional distractor. This suggests that in N10 stimulus competition also played a role in perimetric measurement, causing a failure in the detection of contralesional stimuli. Thus, in N10 perimetric measurement (HRP) has not validly determined the visual field defect and the apparent scotoma resulted from a neglect-specific mechanism (i.e., extinction) and was not caused by a loss of primary visual function.

Bay (1953) assumes that visual extinction can be explained by sensory suppression: Although a lesion in the parietal lobe does not result in hemianopia, it might cause visual percepts to be represented in a weaker fashion in the contra- than in the ipsilesional field. After lesion of one hemisphere there may be a breakdown of a dynamic inter-hemispheric balance based upon disturbed reciprocal inhibition processes (Kinsbourne, 1977, 1993; Olivieri et al., 1999). In the DISTRACTOR condition, hemispheric rivalry occurs and, in case of extinction, the unaffected hemisphere (usually the left one) becomes hyperactive when released from the inhibition by the affected hemisphere. Thus, the weakest sensory signal might not be perceived. Kastner, De Weerd, Desimone, and Ungerleider (1998) studied the influence of competition within one hemifield in healthy subjects using fMRI, and

found reduced activation in visual extrastriate cortex under simultaneous stimulation when compared with sequential stimulation. Also Motter (1993) found neural correlates of focal attentive processes in cortical visual areas V1, V2 and V4 within a field of competing stimuli in a study using single-cell recordings in monkeys. In agreement with current theory they concluded that the analytic mechanisms for processing perceptual features are controlled by "feedback" pathways within the cortex that convey information from higher-order processes like attention. In our patients with neglect, processes due to inter-hemispheric rivalry and backward projections of the lesioned parietal lobe might reduce activation in striate cortex (Roelfsema, Lamme, & Spekreijse, 1998) and in extrastriate cortical areas (Chelazzi, Duncan, Miller, & Desimone, 1998), resulting in a kind of secondary, that is, extinction-induced, anopia.

In summary, competition of simultaneously presented stimuli in chronic neglect patients can be studied by two kinds of paradigms:

First, competition under simultaneous stimulation with a *contralesional target and an ipsilesional distractor*, invokes an attentional component of competition, that is, an ipsilesional shift of attention in chronic neglect patients that is independent of a visual field defect in perimetry. This attentional component can also be observed to some extent in hemianopic patients, where the ipsilesional shift is caused by an attraction of attention to the visible distractor while simultaneously presenting the target in the blind field.

Second, competition under simultaneous stimulation with an *ipsilesional target and a contralesional distractor* suggests the distractor is processed in some of the neglect patients, albeit blocked from awareness. This, in turn, might be explained by sensory suppression that causes a weaker percept of the contralesional stimulus; hyperactivation of the unaffected hemisphere might result in an enhanced transcallosal inhibition of homologous brain areas in the affected hemisphere (Kinsbourne, 1977, 1993; Olivieri et al., 1999). This might lead to a further reduction of activation in striate cortex by backward projections from parietal to occipital brain

areas. The second paradigm may be useful to disentangle hemianopia from neglect within a given patient: when unconscious processing of the distractor is observed in visual field areas of "apparent blindness" (as defined by perimetric testing of a patient with chronic neglect), the failure to respond to contralesional stimuli is due to extinction rather than being caused by hemianopia.

Moreover, the results suggest that neglect patients, unlike pure hemianopics, react differently to removing the fixation point: Disappearing of the fixation point led to an ipsilesional shift of attention in neglect patients and to a contralesional shift in hemianopics. From this we predict that removing the fixation point in standard visual field testing would also lead to a shift of attention into the ipsilesional hemifield in neglect patients, worsening stimulus detection in the defective hemifield.

In all neglect patients, double simultaneous stimulation led to a pronounced increase of RT to contralesional stimuli in comparison to hemianopics. This effect is *independent of the visual field defect* in neglect patients, and presumably caused by inter-hemispheric competition of two stimuli. The fixation point did not constitute such a competitive condition in our group of chronic neglect patients, however. From this, and from our results in the search experiment we conclude that visual field testing with a fixation point is appropriate also for neglect patients.

In about 27% of the neglect patients stimulus detection depended on *eccentricity*. This points to a neglect-specific spatial influence on perimetric measurement, that is, an ipsilesional distortion of the spatial reference frame. For these patients it may be helpful to change testing conditions so that they can be tested with their body turned to the left and gaze turned to the right side (see Kooistra & Heilman, 1989), presumably leading to an overlap of retinal axis and internal body-centered spatial reference axis.

Using double stimulation with a contralesional distractor and an ipsilesional target stimulus allows to test for *unconscious processing* of the distractor. This provides the opportunity to functionally disentangle primary visual defects from pure neglect. With that paradigm we found that

the visual field defect in one patient was rather caused by stimulus competition than by a primary visual defect. The paradigm may thus be useful to disentangle hemianopia from neglect also within a patient.

In conclusion, we showed that patients with chronic neglect often have additional visual field defects that need to be disentangled from neglect characteristics like a rightward attentional shift or the extinction phenomenon. This can be tested using a paradigm of double simultaneous stimulation.

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