

WHEN two visual events appear consecutively in the same spatial location, our response to the second event is slower than that to the first. This inhibition for repeated events may reflect a bias toward sampling novel locations, a bias useful for exploring the visual space. Patients with right hemisphere damage and left neglect explore asymmetrically a visual scene. They are initially attracted by right-sided items and become stuck to them, being unable to reorient their attention toward the left. Here we show that neglect patients show facilitation instead of inhibition for repeated events on the right, non-neglected side. Patients without neglect showed normal inhibition. Our observation may explain why neglect patients' exploration of space cannot extend beyond a few right-sided objects. *Neuro-Report* 10:3353–3357 © 1999 Lippincott Williams & Wilkins.

Key words: Attention; Inhibitory processes; Reaction time; Unilateral neglect

Facilitation instead of inhibition for repeated right-sided events in left neglect

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Introduction

Unilateral neglect is a disabling disorder that often follows right hemisphere lesions. Neglect patients live in a halved world, being unable to orient or respond to events occurring on the left side. In contrast, they show a pathological magnetic attraction toward right-sided objects; as soon as a visual scene unfolds, they orient their attention toward the objects lying on the right side [1]. Previous work with speeded manual responses to lateralized visual targets [2] has shown that the mere appearance of bilateral boxes in which the targets were to appear is capable of further slowing response latencies for left targets, as if the right-sided box attracted patients' attention before the actual targets were shown. If one asks these patients to cross over lines scattered on a sheet, they typically cancel only right-sided lines and may keep cancelling the same lines over and over again. Perhaps normal individuals do not show this repetitive behaviour because of a mechanism that inhibits repeated orientations toward the same event. When attention is summoned by a luminance change in the visual field, targets appearing in that location within ~200 ms are detected faster than targets appearing elsewhere; however, during the following 3 s or more this early advantage turns into a cost and detection becomes slower [3].

This is a robust phenomenon, which can be elicited both in the periphery and at the fovea [4] and is stronger when both repeated events require a motor response [5]. Inhibition affects the display rather than the retinal locus, so that eye movements do not influence it [4,6]. Inhibition occurs even when there is no alternative location at which a target could occur [3], suggesting that it is a true inhibitory effect for the recently attended location, and not a facilitation for other locations resulting from expectancy bias. Though observed also with auditory stimuli, inhibition is greater with visual events, and shows an inverse relationship with target intensity [7]. These characteristics, which parallel attentional phenomena, suggest that inhibition is, at least in part, attentional in nature [7]. In particular, it might be related to reflexive automatic attentional shifts [4]. This form of attentional orienting seems to be particularly impaired in patients with unilateral neglect [1,2,8]. Using a paradigm in which subjects had to respond to a visual target (an asterisk) preceded by a cue (a change in luminance of the box in which the target was to appear), inhibition has been found normal in aged individuals [9] and in patients with focal brain lesions in the frontal, parietal and temporal lobes [10,11], but without severe neglect.

Taking advantage of a simpler reaction time task,

we were able to study 10 patients with moderate to severe unilateral neglect, as defined by performance on a standardized test battery [12]. We compared their performance with that of brain-damaged patients without neglect and that of volunteers without neurological impairment.

Subjects and Methods

Subjects: Ten volunteers without neurological impairment (mean age 56 years), 10 patients with unilateral lesions in the right hemisphere and no evidence of unilateral neglect (mean age 66 years) and 10 right-brain damaged patients with left neglect (mean age 61 years) consented to participate in the experiment. All patients had lesions in the posterior part of the right hemisphere, except two neglect patients, whose lesions were, respectively, in the thalamus and the frontal lobe, and one patient without neglect, who had a subcortical lesion (Table 1, Fig. 1). The three groups of subjects were matched for age ($F(2,27) = 1.99, p > 0.1$) and education (years of schooling; $F(2,27) = 1.66, p > 0.2$). The amount of time elapsed from clinical onset did not significantly differ between the two groups of patients ($F(1,18) = 1.05, p > 0.3$). Three patients with neglect and one patient without neglect had left hemianopia with spared macular vision, which allowed them to perform the reaction time task. Two other neglect patients had left quadrantanopia, one inferior and one superior. Diagnosis of neglect was made clinically and confirmed by a standardized test battery [12], including tasks of line cancellation, identification of lateralized overlapping figures and line bisection. In addition, all patients were asked to cross out 60 letter As scattered on a horizontal A4 sheet and interspersed with distractor letters [13]. On this task, neglect patients found a mean of five targets on the left side (range 0–18) and 24 on the right side (range 22–27). Patients without neglect cancelled a mean of 28 left-sided targets (range 25–30) and 28 right-sided targets (range 27–30).

Procedure: Subjects sat in front of a computer monitor at a distance of ~50 cm. Three horizontally arranged black circles were displayed on a white background, the central circle being located at the centre of the screen (Fig. 2). The circle diameter subtended $\sim 1^\circ 30'$ of visual angle and the distance between circles was $1^\circ 50'$. Subjects were instructed to maintain fixation upon the central circle and to place the index finger of their right hand on the centre of the computer spacebar. After an interval varying randomly from 1000 to 2000 ms, either the right-sided or the left-sided circle became grey. As soon as the target appeared, subjects had to respond

by pressing the spacebar as quickly as possible. They were informed that targets could appear on the left or on the right side with equal probability. Response latencies were measured to the nearest millisecond from target onset to key press by a computer program that sampled the keyboard 2–3 times every millisecond. The target disappeared when a response was made. The experimental session began with six practice trials, during which the investigator made sure that subjects responded to all the targets, if necessary by pointing toward a neglected target. After a short pause, 40 right- and 40 left-sided trials were presented, in a random order.

Data analysis: For each subject and each side of target location (left or right), we selected the first 10 pairs of successive trials that met the following constraints: (1) the target occurred in the same spatial location on both trials; (2) the first target was not preceded by a target in the same spatial location; (3) both response latencies in each pair fell in the range 150–4500 ms. Using these criteria, 10 pairs of trials were examined for each subject and each side of space, with the following exceptions: one control subject, one neglect patient and one brain-damaged patient without neglect had nine pairs for the left side; one control subject, one neglect patient and one non-neglect patient had nine pairs for the right side; one non-neglect patient had nine pairs for both sides.

Results

Figure 3 displays the response latencies for those pairs of trials in which two consecutive targets (T1 and T2) appeared in the same spatial location. T1 always appeared on the opposite side to the previous target, or was the first target of the task. The response of normal individuals to T2 was 82 ms slower than to T1 ($F(1,9) = 11.82, p < 0.01$), consistent with the phenomenon of inhibition for repeated targets. This cost occurred for both right-sided targets (Wilcoxon signed ranks test, $z = -2.59, p < 0.01$) and left-sided targets ($z = -2.49, p < 0.05$), and was shown by nine of the 10 participants. Brain damaged patients without neglect responded faster to right-sided than to left-sided targets ($F(1,9) = 5.47, p < 0.05$), thus revealing a subclinical form of spatial bias [8]; however, similarly to normal individuals, they were 104 ms slower in responding to T2 than to T1 ($F(1,9) = 8.93, p < 0.01$). Inhibition was present for both sides of space; nine of 10 patients showed this repetition cost for left-sided targets ($z = -2.59, p < 0.01$) and eight for right-sided targets ($z = -2.09, p < 0.05$). As expected, patients with left neglect responded faster to right-sided than to

Table 1. Demographic and clinical characteristics of patients

Patient	Sex, age, years of schooling	Onset of illness (days)	Aetiology	Locus of lesion	Letter cancellation (left/right found targets; max. 30/30)	Line bisection (% deviation) ^a	Visual field	Double sensory stimulation
N1	F, 62, 15	90	Ischemic	O,Th	1/26	+50.24	Left hemianopia	Normal
N2	M, 63, 9	91	Hemorrhagic	FT	1/22	+26.19	Left extinction	Left extinction
N3	M, 76, 10	3	Ischemic	TO	9/25	+44.05	Left hemianopia	Normal
N4	F, 76, 6	377	Ischemic	F	12/27	+0.24	Left extinction	Normal
N5	M, 61, 8	135	Traumatic	TP	18/23	+2.86	Normal	Normal
N6	M, 65, 12	52	Hemorrhagic	T (P)	2/23	+3.81	Left extinction	Left extinction
N7	F, 53, 7	76	Ischemic	FP	1/22	+29.52	Left extinction	Left extinction
N8	M, 67, 18	37	Ischemic	Th	0/27	+19.76	Left superior quadrantanopia	Normal
N9	M, 50, 7	306	Ischemic	FTP	7/26	+3.57	Left inferior quadrantanopia	Left extinction
N10	M, 43, 11	44	Traumatic	TP	0/25	+43.33	Left hemianopia	Normal
R1	F, 76, 19	10	Ischemic	FP	29/30	+5.00	Left extinction	Left extinction
R2	M, 58, 20	171	Ischemic	FPO	29/28	-0.71	Left extinction	Normal
R3	M, 75, 18	111	Ischemic	FP	25/28	+1.19	Normal	Left extinction
R4	F, 70, 12	53	Ischemic	FP	26/27	+6.19	Normal	Normal
R5	M, 68, 8	190	Ischemic	FP	27/27	-0.24	Normal	Left extinction
R6	M, 63, 11	10	Ischemic	FP	30/29	+6.19	Normal	Normal
R7	F, 77, 6	8	Ischemic	FP	25/27	-7.38	Normal	Normal
R8	M, 53, 18	39	Ischemic	IC,BG	29/30	0.00	Normal	Left extinction
R9	F, 72, 5	33	Hemorrhagic	FPT	30/30	+8.33	Normal	Normal
R10	M, 57, 5	129	Ischemic	FT,BG	28/30	+7.38	Left hemianopia	Left hemianesthesia

N, patient with left neglect; R, patient without signs of neglect; F, frontal; T, temporal; P, parietal; O, occipital; Th, thalamic; IC, internal capsule; BG, basal ganglia. Parentheses indicate marginal involvement.

^aPositive values indicate rightward shift of the subjective middle; negative values indicate leftward shift.

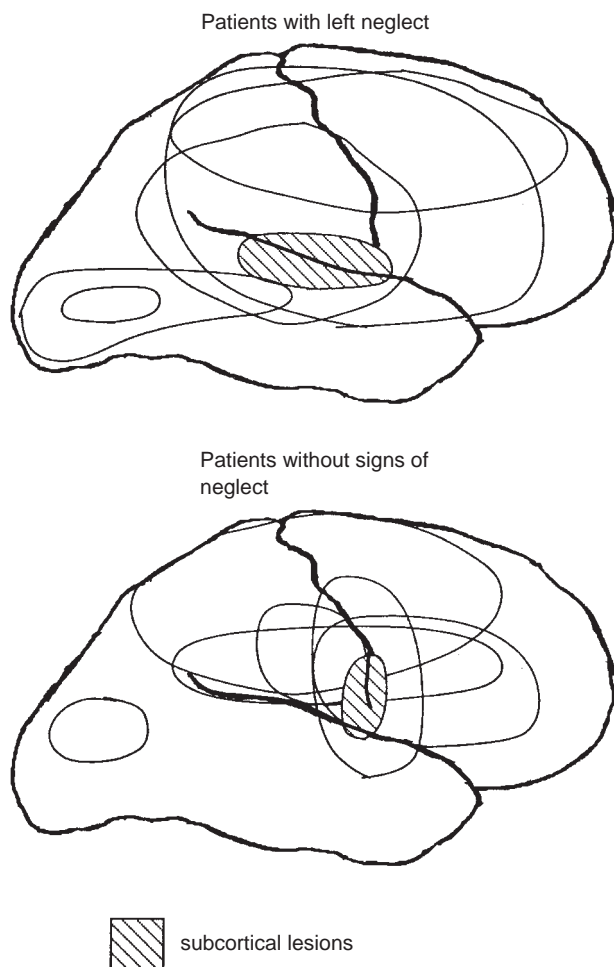


FIG. 1. Schematic reconstruction of the lateral projection of the lesions in six patients with left neglect and in six patients without signs of neglect.

left-sided targets ($F(1,9) = 11.06$, $p < 0.01$). For left-sided targets, five patients showed an advantage and five a cost for T2 vs T1 ($z < 1$). Most importantly, for right-sided targets neglect patients were 80 ms

faster in responding to T2 than to T1 ($z = -2.29$, $p < 0.05$), an advantage shown by nine of 10 patients. Thus, neglect patients showed facilitation instead of inhibition for repeated events on the right side. This result did not depend on a general slowing in performance of neglect patients, because their overall latencies for right-sided targets were similar to those of patients without neglect ($F(1,18) = 1.82$, $p > 0.19$).

Four of the patients without neglect in the present study had recovered from previous neglect; on the other hand, the sole neglect patient who showed inhibition for right-sided targets was receiving rehabilitation for neglect and had no evidence of neglect at a retest 4 months later. Thus, the capacity of inhibiting repeated orienting to right-sided visual events could be important for recovery from left neglect. In fact, significant positive correlations emerged between a normalized score of inhibition (the difference between T2 and T1 response latencies divided by their sum) for right-sided targets and the number of left-sided targets found in line ($r = 0.54$, $p < 0.05$) and in letter cancellation ($r = 0.59$, $p < 0.01$). Thus, the capacity to inhibit successive responses to right-sided events could predict performance on the left side of paper and pencil neglect tests.

Discussion

When a normal individual's attention is attracted by a luminance change, facilitatory and inhibitory mechanisms develop for targets occurring at that location [4,6]. These opposite processes have different time courses, with facilitatory mechanisms prevailing shortly after the first event and inhibitory mechanisms predominating at longer intervals. Our finding that neglect patients present facilitation instead of inhibition for repeated right-sided targets

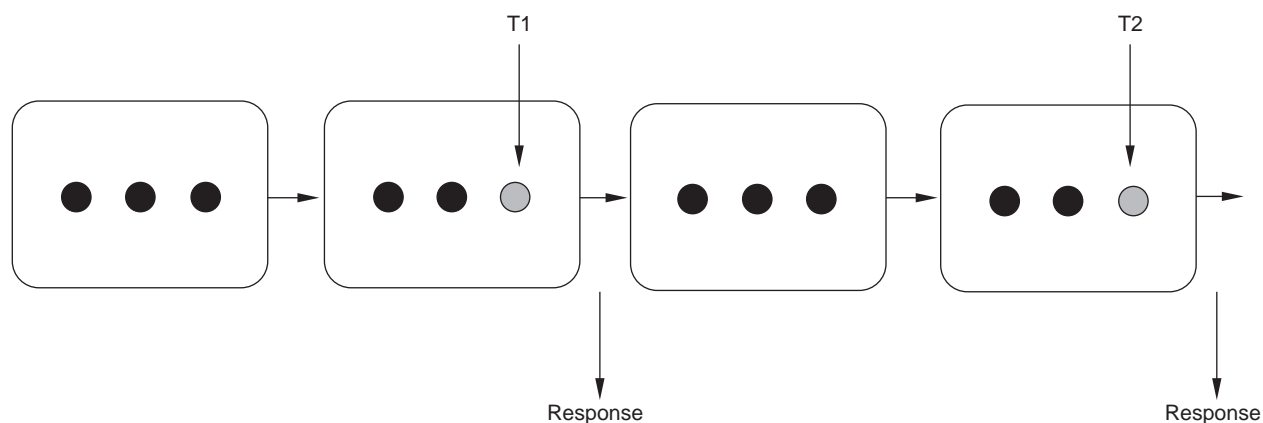


FIG. 2. Example of a same-side sequential pair of trials with two repeated right-sided targets.

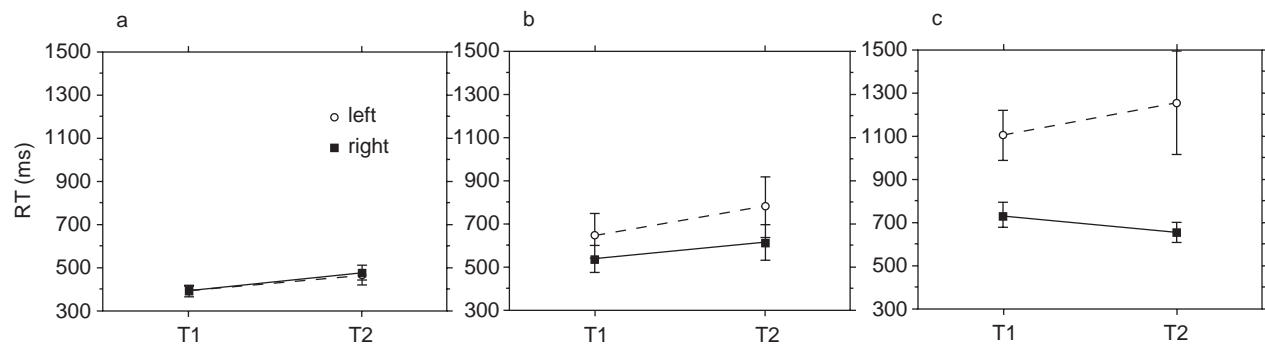


FIG. 3. Response times (RTs) to pairs of consecutive targets occurring in the same spatial location (open symbols, dashed line: left; filled symbols, solid line: right), for normal individuals without brain damage (a) and patients with lesions in the right hemisphere without (b) or with (c) unilateral neglect. Error bars indicate s.e.m.

could reflect a deficit in inhibitory mechanisms, or an abnormally strong facilitatory process, which would overcome inhibition. It has repeatedly been suggested that an important mechanism leading to left neglect is attentional capture from right-sided objects [1,14–16]. Our observation supports this notion and suggests a possible mechanism for this persisting attentional orientation. Minor forms of this deficit could result in the well-known slowing of disengagement from a previously cued location on the side of the brain lesion [17,18]. A non-lateralized slowing of attentional mechanisms [19] might also contribute to the results that we observed by delaying the onset of inhibition beyond the time interval explored in the present study. In any case, the abnormal attentional behaviour that we observed occurred in the right, non-neglected hemispace, thus confirming that even processing of information coming from this apparently unimpaired side is abnormal in neglect [20].

Conclusion

Left unilateral neglect provides an opportunity of studying the brain mechanisms of space processing. It constitutes also a major handicap for neurological patients. A more precise understanding of the mechanisms leading to neglect behaviour is thus important for both research and clinical purposes. We have shown that left neglect patients are unable to inhibit repeated attentional orientations toward the right. This phenomenon occurred in neglect patients, but not in patients with similar brain lesions and no signs of neglect, who showed normal inhibition. Our observation may explain neglect patients' tendency to get stuck to right-sided objects, a tendency

typical of the most severe and invalidating forms of neglect, often resulting in the confinement of the whole patients' behaviour in a reduced portion of space on their extreme right. Efforts to develop an active inhibition for right-sided objects might inspire new rehabilitation techniques for unilateral neglect.

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