

Research report

Effects of same- and different-modality cues in a Posner task: extinction-type, spatial, and non-spatial deficits after right-hemispheric stroke

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Abstract

The response delay to left target stimuli preceded by right-side cues, first described by Posner et al. [J. Neurosci. 4 (1984) 1863–1874] appears to be a stable marker of right-parietal injury. However, only few studies compared patients' performance to age-matched controls. Furthermore, only few studies compared visual and auditory stimuli in this task. Therefore, two groups of right-hemisphere stroke patients, with and without left visual hemineglect, and a healthy control group were studied in three versions of Posner's paradigm. Visual or auditory target stimuli were presented to the subject's left or right, following a visual or auditory cue by 150 ms. The classical 'extinction-type' effect, an increase in missing responses for right visual cue/left visual target, was specifically observed in neglect patients. In the same condition, an 'extinction-type' response delay was present in patients with neglect and in those without neglect. No such delay occurred in any group when cues were auditory. Specifically in neglect patients, response times were generally longer for left than for right visual targets, regardless of cue side and of cue modality. Response times were generally prolonged in neglect patients regardless of target modality. This suggests that three components impair neglect patients' performance in this paradigm: a non-spatial, supramodal deficit, a global, neglect-type deficit of the contralesional hemi-field, and the extinction-type impairment. The latter two deficits appear to be most marked within the visual domain.

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1. Introduction

Spatially based selection, a key process in human perception, is characteristically impaired in patients with right-hemispheric brain lesions suffering from a hemineglect syndrome. Hemineglect, or briefly 'neglect', is defined as a lack of awareness and responses to events that occur in the left half of the visual field, of space, of objects, and of the patient's own body (see Refs. [12,18,19,29,37] for recent reviews). The neglect syndrome may or may not be

associated with an extinction phenomenon [7], i.e. on simultaneous presentation of left and right stimuli, only right-field stimuli elicit proper responses. Extinction is usually regarded as a component of the neglect syndrome but some authors consider both entities as separate: neglect as a disorder of spatial representation and extinction as a deficit of attentive vision ([24,38], see also case report in Ref. [9]).

To make extinction accessible to methods and concepts from experimental psychology [26], a cue–target task was introduced by Posner et al. [27] where response time was the variable of primary interest: Patients have to respond to visually presented 'target' stimuli with a keypress, no matter whether targets occur left or right. Targets are announced by same-side ('valid') or opposite-side ('in-

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valid') visual 'cues'. The major finding emphasised by Posner et al. [27] was a delay of right parietally lesioned patients' reaction times to the combination right cue/left target, replicated e.g. in Refs. [1,14,16,39]. This finding reminds very much of the extinction phenomenon, so it was labelled 'extinction-type pattern' by Posner et al. [27]. In fact, it might be slightly different from the classical phenomenon of visual extinction which is most marked with simultaneous left–right stimulation [4] whereas the response-time delay in Posner's paradigm has been obtained over cue–target asynchronies from 50 to 1000 ms [1,14,27]. Furthermore, the extinction-type pattern could be obtained even in patients in which neglect, as measured by standard clinical tests, was almost [39] or entirely [16] absent, though previously present in some of these patients. In any case, whatever the relations of this extinction-type pattern are to other variants of extinction and to neglect in general, this response-time delay appears to be a most sensitive and stable marker, easily and precisely quantifiable. Insofar as extinction is measured by this effect, these findings are compatible both with the assumption that extinction can be the residual symptom of neglect, and with the assumption that extinction might be something different from neglect.

In the Posner et al. study, this extinction-type pattern was embedded in several other effects (Since the effects were much more prominent in patients with right than with left hemispheric lesions, for simplicity we will develop our argument as if only right hemisphere lesions had been studied):

- First, there was a general '*validity effect*': patients' responses were delayed not only to invalidly compared to validly cued left targets, but also slightly to invalidly compared to validly cued right targets. For brief cue–target intervals this validity effect was also found in age-matched healthy participants [1] and in patients who did not show the extinction-type pattern [16].
- The second embedding effect [1,8,14,16,27,28] was a '*target-side effect*': patients' responses were not only delayed to left targets that were invalidly cued but also to left targets that were validly cued, when compared to right targets. This effect might reflect generally reduced attention to anything occurring in the left visual hemifield, in addition to the extinction-type pattern.
- A further effect became evident in studies where age-matched healthy participants were included [1,39]: a *general delay* of parietal patients' responses, even for targets in the ipsilesional hemifield.

Therefore, response times to invalidly cued left targets might be delayed due to four components adding to each other:

1. A general delay, affecting responses to all stimuli;
2. A target-side effect, affecting responses to all left-side stimuli;
3. A validity effect, affecting responses to all invalidly cued stimuli;
4. The specific extinction-type delay of invalidly cued left stimuli.

The present study set out to investigate how specific these four effects are to the performance of neglect patients and to the visual cue–target task.

1.1. Specificity to neglect

We know of no study that investigated the cue–target task in groups of patients with neglect, patients without neglect, and age-matched controls, though several studies used two of these three groups, e.g. Refs. [1,8,39]. Testing all three groups was expected to show which of the mentioned effects is specific to neglect, which is specific to right-hemisphere damage in general, and which is present even in healthy elderly subjects. We expected from previous literature:

- An extinction-type pattern in patients with and without neglect [16], but not in healthy elderly,
- A validity effect in all groups alike,
- A target-side effect in patients with neglect only or at least more than in other patients [16,34],
- A general delay of responses in both groups of patients which, according to previous studies [30,34], should be more pronounced in neglect patients.

1.2. Specificity to visual stimuli

Farah et al. [14] reported a response delay with invalidly cued left visual targets also in case of auditory cues in a modified Posner paradigm. Using auditory cues we aimed at replicating this effect. Auditory cues might well draw patients' attention towards their side and then prevent contralateral targets from being attended. This would be true if the extinction-type phenomenon is based on the location of cues and targets in 'supramodal' space or if there is transfer from auditory space to visual space [11,13,36].

Alternatively extinction might not simply be due to attention being drawn right and left, as extinction of stimulus detection has been shown to heavily depend on the similarity of right-side and left-side visual stimuli [3,41]. In this case, the extinction-type pattern should disappear with auditory cues because e.g. a right-side auditory cue and a left-side visual target certainly share less similar features than any two dissimilar visual stimuli presented by Baylis et al. [3].

An alternative reasoning leading to the prediction that the extinction-type pattern should disappear with auditory cues is that isolated auditory events cause more arousal than visual events. If such auditorily induced arousal would indeed alleviate patients' extinction [31], any specific effect of cue side might disappear.

Finally, subgroups of participants were also tested with visual cues and auditory targets. In principle, the same considerations made above for auditory cues and visual targets apply to this setup of stimuli. So again we were interested whether the extinction-type pattern would occur, and further, whether auditory stimuli used as targets would also give rise to the neglect-type pattern, with responses being delayed to all left-side targets irrespective of cue.

To keep the design as simple as possible, we focused on only one cue–target interval and on one predictive value of the cues (unlike most previous studies), for two reasons: (1) A cue–target interval of 150 ms was chosen to make cues and targets interact with respect to reflexive shifts of attention only [25], and cues had validity of 50% throughout, therefore were unpredictable for targets, precluding conscious allocation of attention (see Refs. [2,5,21] for

details about automatic and controlled attention in the hemineglect syndrome). (2) The short cue–target interval also served to minimize a possible contribution from eye movements (as suggested by Posner et al. [28], see Verleger et al. [40] for experimental data on the role of eye movements in this task).

2. Methods

Three groups of subjects took part in the study with informed consent and approval of the local ethics committee:

- Neglect group (N+; see Table 1a):

Thirteen patients aged 35–78 years (median 64 years; seven females) with right-hemispheric ischemia or hemorrhage (confirmed in CT and/or MRI, in most cases at temporo-parietal, posterior parietal, fronto-precentral, or basal ganglia location, lesion-to-test interval 1–29 weeks, median 14 weeks) and left visual hemineglect syndrome (score below 166 in the German version of the Behavioural

Table 1
Sites of lesions in (a) Neglect group and (b) Patients without neglect group (all lesions right-hemispheric)

Patient	Age/sex	(Pre)-frontal lesions	(Pre)-central lesions	Posterior parietal lesions	Lesions of the temporo-parietal junction	Temporal lobe lesions	Occipital lesions	Basal ganglia lesions	Pyramidal tract/internal capsule lesions	BIT	Lesion-to-test interval (weeks)
<i>(a) Neglect group</i>											
1	72 f			+	+				(+)	116	11
2	78 f			+	++					156	29
3	50 f		(+)	+	(+)			+		125	n.a.
4	72 f			+	+					116	20
5	77 m				+		+ (h)	+	(+)	84	6
6*	64 m	++	++	++	++					96	29
7	68 m	+	+		+					151	1
8*	77 f				(+)			+		129	2
9	35 m	++	++	++	++			++	++	160	22
10	47 m	(+)	++	++						149	7
11	60 f	(+) (h)						++ (h)		157	14
12	51 m	+	++	+	+	+		(+)		154	n.a.
13	60 f		+	(+)	+			+		148	13
<i>(b) Patients without neglect group</i>											
1	52 m	++	(+)			++			+	168.5	28
2	58 f					+		+	+	170	12
3	55 f	(+)				(+)		+	(+)	169	13
4	60 f					+		(+)	+	168.5	233
5	50 f							+	+	169	12
6	68 f	+	(+)						(+)	168	24
7	62 m	+(sh)				(+)				169.5	6
8	72 m		(+)			(+)				167.5	40
9	60 m	+								169.5	5
10	62 m					(+)		+		169.5	6
11	61 m	(+)	(+)							169	13

BIT, score in Behavioural Inattention Test (167–170: no neglect; 136–166: moderate neglect; 73–135: severe neglect); lesion-to-test interval in weeks (n.a., not available). (+)=minor involvement by the lesion; +=partial involvement by the lesion; ++=complete involvement by the lesion; (h)=hemorrhage; (sh) minor secondary hemorrhage; * data discarded (misses >80%, see Section 2).

Inattention Test, BIT¹ [42], measured on-site immediately after the experiment; median 148; range 84–160).

- Patients without neglect group (N–; see Table 1b):

Eleven patients aged 50–72 years (median 60 years; five females) with right-hemispheric ischemia or hemorrhage. Lesions were at prefrontal, (centro-)temporal, anterior temporal, strio-lenticular, or capsular locations, sparing the classical neglect-inducing lesion sites, such as the posterior parietal lobe, the temporo-parietal junction, and in most cases also the fronto-precentral region around the frontal eye fields (confirmed in CT and/or MRI, lesion-to-test interval 5 weeks to 4.5 years, median 13 weeks). In these patients there was no hemineglect syndrome at the time of investigation (BIT score: median 169; range 167.5–170) and no history of a past hemineglect syndrome.

- Control group (C):

Eighteen persons aged 52–92 years (median 61 years; 11 females) without history of neurological disorder.

In all participants, visual acuity was measured immediately before the experiment and found to be better than 0.7.

Subjects were seated comfortably in a chair in a dimly illuminated sound-protected room. A response-button was fixed on the right armrest of the chair such that it could be comfortably pressed with the right index finger.

Visual stimuli were presented on a computer screen (viewed from 1.5 m distance). For optimal precision, the screen refresh was time-locked with the reaction time measurement.

Auditory stimuli were presented via earphones, either to the left or to the right ear. Before the experiment, sound intensity was adjusted to a level of approximately 77 dB. Subjects reported this intensity to be comfortable, with left-ear and right-ear stimuli being easily hearable. Headphones were preferred to loudspeakers for two reasons. First, they permitted easy individual adjustment of sound intensity, separate by ear, to ensure that sounds were perceived as equally loud on both sides. Second, results of pilot work (based on Mills's study [23] of earphone- vs. loudspeaker-delivered 2000 Hz tones resulting in similar detection of interaural intensity differences) were as follows: in the present setting, earphones permitted an easy discrimination left/right, in contrast to loudspeakers placed near the locations where the visual stimuli were presented (see below: ≈ 20 cm apart from each other at a distance of 1.5 m, $\approx 8^\circ$). These two reasons outweighed the dis-

advantage that auditory and visual stimuli were not spatially coincident.

Visual and auditory stimuli were presented in three blocks of 200 trials each during a single experimental session (with breaks given when needed) in the following sequence:

Visual cue–visual target, VC/VT (with minor modifications the same stimuli as in Ref. [39]):

Throughout the experiment, a light gray dot-shaped fixation mark was shown in the centre of the dark-gray screen. On each side of the fixation mark, the outlines of two rectangles were presented ($\sim 1.5^\circ$ wide and $\sim 1.3^\circ$ high; inner edges $\sim 3.1^\circ$ from the centre of the screen). By default, the frames of the rectangles were light gray. The cue, given once every 3.2–3.6 s, consisted of one of the rectangle frames turning yellow (and remaining so until the end of the trial). A further 150 ms later, the target was presented, consisting of a light gray diagonal cross presented in one of the two rectangles. The trial ended 1850 ms later, with the screen returning to the default configuration (gray rectangles without diagonal cross, dot-shaped fixation mark).

Cue and target stimuli were presented in one of the following combinations: LL (left cue, left target, 'validly cued' or 'valid' for brevity), RR (right cue, right target, 'valid'), LR (left cue, right target, 'invalid'), RL (right cue, left target, 'invalid'), 50 trials in each combination (equal probability of 25%) in random order.

Subjects were instructed to press a button with their right index fingers as soon as the target appeared. A total of 10–20 practice trials were given before the experiment started. Reaction times, referred to target onset, were recorded and averaged separately for each cue–target combination. Reaction times above 1850 ms after target onset were defined as 'misses' (assuming that later reactions might be not sufficiently specific to the stimuli). Trials where the button was pressed before target onset were discarded; these premature-response trials were removed from the set of trials, thus reducing the total number of trials. For technical reasons no catch trials could be included (see Section 4). The number of misses will be given in % of the total number of trials.

Auditory cue–visual target, AC/VT:

Same as VC/VT (cue–target interval 150 ms), but instead of the visual cue, a 2000-Hz tone of 150 ms duration was presented to the left or right ear. As no visual cue was given, frames of rectangles remained gray throughout the trial.

Visual cue–auditory target, VC/AT:

Same as VC/VT (cue–target interval 150 ms), but

¹The Behavioral Inattention Test (BIT) consists of six 'conventional' tests (e.g. line bisection, line cancellation, star and letter cancellation, figure and shape copying) and nine 'behavioral' tests (e.g. telephone dialing, reading, visual exploration of natural scenes, telling and setting the time on a clockface). For details see Ref. [42].

instead of a visual target, a 2000-Hz tone of 1850 ms duration was presented to the left or right ear. Like in VC/VT, the frame of the rectangle that had been highlighted as a cue remained yellow until the end of the trial.

Data from two neglect patients were discarded because the number of misses was so high (>80% in at least one of the subconditions with left targets) that reaction times could not be determined reliably. For statistical evaluation, ANOVAs were performed using the GLM module in SPSS 9.0. The first analysis focussed on the VC/VT task (ANOVA-1a). Factors used were Validity of the cue (VALIDITY: valid, invalid; within-subject), Target Side (TARGET: left, right; within-subject) and Group (GROUP: N+, N-, C; between-subjects). Then the VC/VT pattern of results was compared to AC/VT and to VC/AT in two separate analyses (ANOVA-1b and -1c), by adding the factor Condition (CONDITION: VC/VT vs. AC/VT in one analysis, VC/VT vs. VC/AT in the other analysis; within subject). Comparison of VC/VT vs. AC/VT was separated from comparison of VC/VT vs. VC/AT for two reasons:

1. Data for both VC/VT and AC/VT were available in N=11/11/16 subjects (N+/N-/C) whereas data for both VC/VT and VC/AT were available only in N=6/10/14 subjects; given this, using CONDITION as a three-level factor would have led to all participants without VC/AT data being dropped from AC/VT analysis;
2. Effects of CONDITION could be interpreted more unambiguously when CONDITION was a two-level rather than a three-level factor.

We will focus on interactions of CONDITION, VALIDITY, and TARGET with GROUP. To resolve these interactions, effects of VALIDITY and TARGET were tested separately for each task in each group (ANOVA-2). Effects with $P < 0.05$ were regarded as significant. Tendencies ($0.05 < P < 0.10$) will be reported as well.

3. Results

Reaction times and rates of misses (mean values) are shown in Fig. 1. Results for VC/VT will be reported first. AC/VT and VC/AT data will be presented in comparison with VC/VT. For each condition, results will be presented grouped by the four hypothesized effects listed above:

1. General delay, denoted by 'a' in Fig. 1
2. Target-side effect, denoted by 'b' in Fig. 1
3. Validity effect
4. Extinction-type delay, denoted by 'c' in Fig. 1

Results of statistical tests are summarized in Table 2 (F -values for ANOVA-1a, VC/VT only, and ANOVA-1b,c: VC/VT vs. VC/AT and VC/VT vs. AC/VT) and Table 3 (F -values for ANOVA-2, effects of VALIDITY and TARGET only, separated by group N+, N-, and C).

3.1. Visual cues and visual targets (VC/VT, Fig. 1, top row and Tables 2 and 3, left blocks; N=11/11/16 subjects in groups N+/N-/C)

(1) *General delay*: Reaction times were longer (Fig. 1, left column) and number of misses (Fig. 1, right column) larger in neglect patients than in the control group, patients without neglect being in-between, though not significantly different from controls (factor GROUP for reaction times: $P = 0.002$, Table 2; post-hoc Tukey-HSD tests: N+ vs. C, $P = 0.001$, N+ vs. N-, $P = 0.09$, N- vs. C, n.s.; factor GROUP for misses: $P < 0.001$, Table 2; post-hoc $P < 0.001$, $P < 0.001$, n.s., respectively).

(2) *Target side* had effects both on response times ($P < 0.001$) and on misses ($P = 0.001$, Table 2) and, of particular interest, these effects differed between groups (TARGET×GROUP for response times: $P < 0.001$; for misses: $P < 0.001$, Table 2). Unexpectedly, healthy subjects responded to left targets, on average, 18 ms later than to right targets ($P < 0.001$, Table 3). This result might be related to an interhemispheric transmission delay, as all responses were given by moving the right index finger, thus requiring callosal transmission of left-hemifield visual information from the right occipital cortex to the left motor cortex. This finding will not be discussed further (for details and alternative explanations, see e.g. Ref. [17] and references therein). Left and right targets did not differ in the number of misses for healthy subjects (n.s., Table 3). Neglect patients responded much slower to left than to right targets (difference on average 155 ms, $P < 0.001$, Table 3) and missed more left targets ($P = 0.009$, Table 3; difference in misses for left vs. right targets negatively correlated with BIT score, Pearson's $r = -0.68$, $P = 0.021$). This was not the case in patients without neglect (n.s. for response times and for misses, Table 3).

(3) *Effects of validity*: Responses were slower to invalidly than to validly cued targets (VALIDITY: $P < 0.001$, Table 2), without group difference (VALIDITY×GROUP, n.s., Table 2; effects of validity in each group: N+: $P = 0.03$; N-: $P = 0.006$; C: $P = 0.002$, Table 3).

For missing responses, however, the validity effect differed between groups (VALIDITY×GROUP, $P < 0.001$, Table 2): There was a significant effect in neglect patients only, who missed more invalidly than validly cued targets whereas no such effects occurred in patients without neglect and in the healthy group (N+: $P = 0.002$, N-: n.s., C: n.s., Table 3).

(4) *Interaction of validity and target side ('extinction-type pattern', see arrows in Fig. 1, top row)*: For response

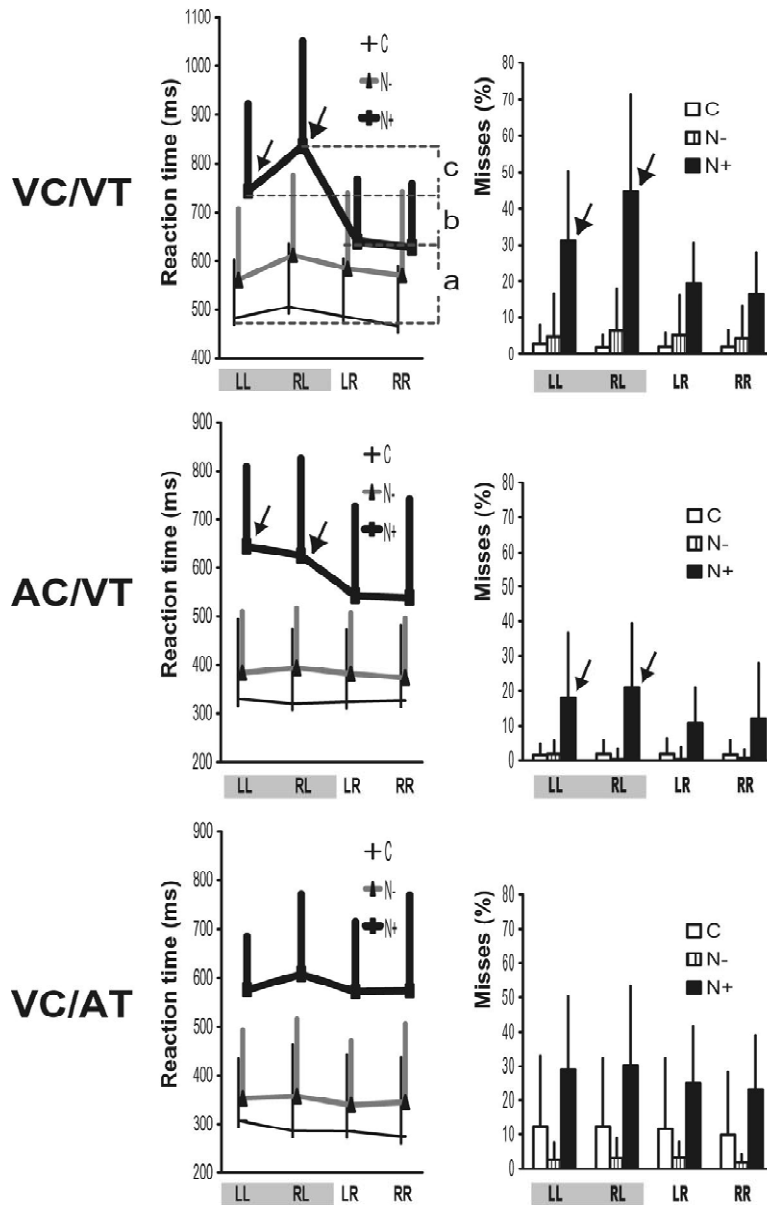


Fig. 1. Left, reaction times (ms after target onset), and right, rates of misses (in percent) in neglect group (N+), ‘patients without neglect’ group (N–), and control group (C), in conditions VC/VT (visual cue/visual target; N=11/11/16), AC/VT (auditory cue/visual target, N=11/11/16), and VC/AT (visual cue/auditory target, N=6/10/14). Note different offset across conditions for reaction time graph. Arrows show the different cue-dependence of left target data in VC/VT vs. AC/VT in the stroke with neglect group. Labels for left targets highlighted for orientation. Labels a, b, and c in the top left diagram (VC/VT, reaction times) denote the three relevant effects to be separated by analysis of variance: Neglect patients’ response times to RL are largest because they are larger than LL (‘c’), both are larger than LR and RR (‘b’) and all four values are larger than response times of the control group (‘a’). ‘a’ is captured by the main effect of GROUP, ‘b’ by TARGET SIDE×GROUP, ‘c’ by VALIDITY×TARGET SIDE×GROUP.

times, the dependence of the validity effect on target side tended to differ between groups (TARGET×VALIDITY×GROUP: $P=0.09$, Table 2): The validity effect was asymmetric, forming the extinction-type pattern. The extra delay for invalidly cued targets was larger for left than right targets both in patients with neglect (replicating the classical extinction-type effect as a tendency) and in patients without neglect but not in healthy subjects

(TARGET×VALIDITY: N+: $P=0.08$, N–: $P=0.05$; C: n.s., Table 3).

For missing responses, the respective interaction was highly significant (TARGET×VALIDITY×GROUP: $P=0.006$, Table 2). However, here the difference was between neglect patients, who missed more invalidly cued targets when on the left (replicating the classical extinction-type effect), and the other two groups where this was not the

Table 2
Results of ANOVA-1 (see Section 2) for response times and misses (italics)

VC/VT			VC/VT vs. AC/VT			VC/VT vs. VC/AT		
			CONDITION (COND, AC/VT vs. VC/VT)	<i>F(1,35)</i>	<i>53.2***</i>	CONDITION (COND, VC/AT vs. VC/VT)	<i>F(1,27)</i>	<i>32.3***</i>
GROUP (GRP)	<i>F(2,35)</i>	<i>7.7**</i> <i>18.1***</i>	GRP×COND	<i>F(2,35)</i>	<i>0.7^{ns}</i> <i>4.7**</i>	GRP×COND	<i>F(2,27)</i>	<i>0.3^{ns}</i> <i>1.8^{ns}</i>
TARGET SIDE (TGT)	<i>F(1,35)</i>	<i>39.4***</i> <i>14.9***</i>	TGT×COND	<i>F(1,35)</i>	<i>6.4*</i> <i>6.0*</i>	TGT×COND	<i>F(1,27)</i>	<i>11.6***</i> <i>4.6*</i>
TGT×GRP	<i>F(2,35)</i>	<i>20.9***</i> <i>11.5***</i>	TGT×GRP×COND	<i>F(2,35)</i>	<i>2.8(*)</i> <i>4.5*</i>	TGT×GRP×COND	<i>F(2,27)</i>	<i>7.8**</i> <i>6.2**</i>
CUE VALIDITY (VAL)	<i>F(1,35)</i>	<i>24.1***</i> <i>18.8***</i>	VAL×COND	<i>F(1,35)</i>	<i>15.6***</i> <i>8.9**</i>	VAL×COND	<i>F(1,27)</i>	<i>4.1*</i> <i>2.4^{ns}</i>
VAL×GRP	<i>F(2,35)</i>	<i>1.5^{ns}</i> <i>16.5***</i>	VAL×GRP×COND	<i>F(2,35)</i>	<i>1.7^{ns}</i> <i>7.1**</i>	VAL×GRP×COND	<i>F(2,27)</i>	<i>0.4^{ns}</i> <i>5.0**</i>
TGT×VAL	<i>F(1,35)</i>	<i>6.6*</i>	TGT×VAL×COND	<i>F(1,35)</i>	<i>12.5***</i> <i>1.9^{ns}</i>	TGT×VAL×COND	<i>F(1,27)</i>	<i>0.6^{ns}</i> <i>7.8**</i>
TGT×VAL×GRP	<i>F(2,35)</i>	<i>2.5(*)</i> <i>6.0**</i>	TGT×VAL×GRP×COND	<i>F(2,35)</i>	<i>3.7*</i> <i>1.4^{ns}</i>	TGT×VAL×GRP×COND	<i>F(2,27)</i>	<i>0.2^{ns}</i> <i>2.4^{ns}</i>

(*) $P < 0.1$, * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Left block: ANOVA-1a on VC/VT data with factors VALIDITY (VAL: valid, invalid; within-subject), TARGET (TGT: left, right; within-subject) and GROUP (GRP: N+, N-, C; between-subjects; N=11, 11, 16).

Middle block: ANOVA-1b, comparison of VC/VT with AC/VT, factors as in ANOVA-1a with CONDITION added (COND: VC/VT vs. AC/VT, within-subject, N=11, 11, 16).

Right block: ANOVA-1c, comparison of VC/VT with VC/AT, factors as in ANOVA-1a with CONDITION added (COND: VC/VT vs. VC/AT, within-subject, N=6, 10, 14).

case (TARGET×VALIDITY: N+: $P=0.02$; N-: n.s.; C: n.s., Table 3).

3.2. VC/VT in comparison with auditory cues and visual targets (VC/VT vs. AC/VT, Fig. 1, middle row; F-values in Tables 2 and 3, middle blocks; N=11/11/16 subjects in groups N+/N-/C)

(1) General delay: Reaction times (Fig. 1, left column) were faster throughout in AC/VT than in VC/VT (CONDITION: $P < 0.001$, Table 2), but the pattern of response times (neglect patients > stroke patients without neglect ≥ controls) was not different between AC/VT and VC/VT (GROUP×CONDITION: n.s., Table 2).

Likewise, number of misses (Fig. 1, right column) was generally smaller in AC/VT (CONDITION: $P=0.001$, Table 2). It was only in neglect patients that a relevant number of misses was observed, resulting in a significant interaction of GROUP×CONDITION ($P=0.02$, Table 2).

(2) Effects of target side: Response times: Like in VC/VT, neglect patients' responses were slower to left than to right targets also in AC/VT ($P < 0.001$, Table 3) though the effect was numerically smaller. The unexpected effect of target side on the healthy group found in VC/VT was no longer there in AC/VT (n.s., Table 3). Thus, effects of target side were smaller in AC/VT than VC/VT both for the neglect patients and for the control group, leading to interactions of TARGET×CONDITION ($P=$

Table 3
Results of ANOVA-2 (see Section 2) for response times and misses (italics)

VC/VT	AC/VT				VC/AT						
	N+ <i>F(1,10)</i>	N- <i>F(1,10)</i>	C <i>F(1,10)</i>		N+ <i>F(1,10)</i>	N- <i>F(1,10)</i>	C <i>F(1,15)</i>	N+ <i>F(1,5)</i>	N- <i>F(1,9)</i>	C <i>F(1,13)</i>	
TGT	<i>23.8***</i> <i>10.3**</i>	<i>1.2^{ns}</i> <i>1.7^{ns}</i>	<i>20.5***</i> <i>0.2^{ns}</i>	TGT	<i>28.8***</i> <i>6.2*</i>	<i>3.5(*)</i> <i>3.0^{ns}</i>	<i>0.0^{ns}</i> <i>0.2^{ns}</i>	TGT	<i>1.0^{ns}</i> <i>2.3^{ns}</i>	<i>0.5^{ns}</i> <i>0.5^{ns}</i>	<i>1.1^{ns}</i> <i>4.3(*)</i>
VAL	<i>6.1*</i> <i>17.7**</i>	<i>11.8**</i> <i>0.6^{ns}</i>	<i>13.1**</i> <i>0.6^{ns}</i>	VAL	<i>0.2^{ns}</i> <i>0.0^{ns}</i>	<i>3.3(*)</i> <i>2.0^{ns}</i>	<i>1.5^{ns}</i> <i>0.8^{ns}</i>	VAL	<i>0.4^{ns}</i> <i>1.0^{ns}</i>	<i>0.8^{ns}</i> <i>3.1^{ns}</i>	<i>0.1^{ns}</i> <i>1.0^{ns}</i>
TGT×VAL	<i>3.9(*)</i> <i>8.5**</i>	<i>4.7*</i> <i>0.2^{ns}</i>	<i>0.1^{ns}</i> <i>0.4^{ns}</i>	TGT×VAL	<i>0.7^{ns}</i> <i>1.2^{ns}</i>	<i>0.1^{ns}</i> <i>2.4^{ns}</i>	<i>0.2^{ns}</i> <i>0.1^{ns}</i>	TGT×VAL	<i>0.3^{ns}</i> <i>0.1^{ns}</i>	<i>0.6^{ns}</i> <i>0.0^{ns}</i>	<i>0.8^{ns}</i> <i>2.5^{ns}</i>

(*) $P < 0.1$; * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Interactions of CONDITION, VALIDITY, and TARGET with GROUP in ANOVA-1 were resolved by testing effects of TARGET (TGT) and VALIDITY (VAL) separately for each task (VC/VT, AC/VT, and VC/AT) in each group (N+, N-, C).

0.02, Table 2) and, as a tendency, of TARGET×GROUP×CONDITION ($P=0.07$, Table 2).

Misses: Like in VC/VT, only neglect patients missed more left than right targets in AC/VT ($P=0.03$, Table 3). The effect was smaller than in VC/VT, leading to a TARGET×CONDITION interaction ($P=0.02$, Table 2), and the effect occurred in neglect patients only, leading to a TARGET×GROUP×CONDITION interaction ($P=0.02$, Table 2).

(3) *Effect of validity: Response times:* In contrast to VC/VT, there was no delay due to invalid cueing in AC/VT, leading to a highly significant VALIDITY×CONDITION interaction ($P<0.001$, Table 2). This effect was observed for all three groups alike (VALIDITY×GROUP×CONDITION: n.s., Table 2).

For missing responses, this was similar (VALIDITY×CONDITION: $P=0.005$, Table 2) and since missing responses were only relevant in neglect patients the VALIDITY×GROUP×CONDITION interaction was also significant ($P=0.003$, Table 2).

(4) *Interaction of validity and target side: Response times:* Similar to the lacking main effect of validity in AC/VT there was also no special delay for invalidly cued left targets ($F=0.7$, 0.1, and 0.2 for the three groups in AC/VT, Table 3). Because the effect had been present in patients with and without neglect in VC/VT, significant TARGET×VALIDITY×CONDITION ($P=0.001$, Table 2) and TARGET×VALIDITY×GROUP×CONDITION ($P=0.03$, Table 2) interactions were observed.

For misses, these interactions did not become significant (Table 2) because there was still a weak tendency in neglect patients (the only group relevant for misses) for more misses to invalidly cued left targets in AC/VT, though far from reaching significance ($F(1,10)=1.2$, Table 3).

3.3. *VC/VT in comparison with visual cues and auditory targets (VC/VT vs. VC/AT, Fig. 1, bottom row; F-values in Tables 2 and 3, right blocks; N=6/10/14 subjects in groups N+/N-/C)*

(1) *General delay: Response times* (Fig. 1, left column) were faster throughout in VC/AT than in VC/VT (CONDITION: $P<0.001$, Table 2). Again, the pattern of effects (neglect patients>stroke patients without neglect≥controls) was not significantly different from VC/VT (GROUP×CONDITION: n.s., Table 2).

For misses (Fig. 1, right column), no differences in the general level were found between conditions (CONDITION: n.s.; GROUP×CONDITION: n.s., Table 2).

(2) *Effects of target side: Response times:* Unlike in VC/VT, there was no effect of target side in VC/AT (Table 2), leading to significant TARGET×CONDITION ($P=0.002$, Table 2) and TARGET×GROUP×CONDITION ($P=0.002$, Table 2) effects.

For misses, the same was true: TARGET×

CONDITION: $P=0.04$, TARGET×GROUP×CONDITION: $P<0.006$ (Table 2), TARGET effect in neglect patients' VC/AT data: n.s. (Table 3).

(3) *Effects of validity: Response times:* There was also no delay due to invalid cueing in VC/AT (Table 3), in contrast to VC/VT, leading to a VALIDITY×CONDITION interaction ($P=0.05$, Table 2), for all three groups alike (VALIDITY×GROUP×CONDITION: n.s., Table 2).

For missing responses, this was similar, with VALIDITY×GROUP×CONDITION being significant ($P=0.01$, Table 2) because missing responses were only relevant in neglect patients.

(4) *Interaction of validity and target side: Response times:* There was also no significant additional delay for invalidly cued left targets in VC/AT ($F<1.0$ in each group in VC/AT, Table 3) but, though not significant, the neglect patients' mean response times were numerically largest with invalidly cued left targets in VC/AT, similar to VC/VT (Fig. 1), therefore the interactions of TARGET×VALIDITY×CONDITION and of TARGET×VALIDITY×GROUP×CONDITION did not become significant (Table 2).

For missing responses, results were less ambiguous: There were not more missing responses with invalidly cued left targets in VC/AT than with invalidly cued right targets. In line with this, the TARGET×VALIDITY×CONDITION interaction was significant ($P=0.009$, Table 2) and the TARGET×VALIDITY×CONDITION×GROUP interaction approached significance ($P=0.10$, Table 2).

4. Discussion

This study had two main results. First, right-hemispheric stroke and neglect patients' deficits in the visual cue–target task introduced by Posner et al. [27], here with 150 ms cue–target interval, were shown to be composed of several factors. Second, auditory stimuli that replaced the visual stimuli as cues or targets in this task had no side-specific effects.

4.1. Four effects in the visual task

Confirming what was outlined in Section 1 on the basis of previous evidence, indeed four effects affected patients' responses to invalidly cued left targets: a general delay, a general validity effect, a general effect of target side, and the specific effect to invalidly cued left targets:

1. Independent of cue side and target side, patients' responses were generally delayed: Patients with neglect were slowest, the control group was fastest, and patients without neglect ranged in-between though not

statistically different from the control group. This general delay might reflect generally slowed perceptual processes. However, perception-related components of event-related potentials are not delayed in such patients (e.g. Refs. [20,39]; but see Ref. [35]). Recent literature [6,10,32] suggests a non-spatial, non-lateralized deficit of sustained attention or alertness in patients with right parietal lesions as the most probable interpretation.

2. All three groups alike responded somewhat slower to invalidly than to validly cued targets, both left-side and right-side ones. As shown by Bartolomeo et al. [1], this effect is not as unspecific as it might appear from the present data but rather depends on the predictive validity of the cues and on the cue–target interval. However, for non-predictive cues and the short cue–target asynchrony as used here, the present results are in good accordance with those previous findings, reflecting the cost induced by shifting attention towards the invalid cue.
3. Patients had a marked delay of their responses to all left-side targets, both validly and invalidly cued, in agreement to previous evidence [1,8,14,16,27,28]. The present data made two additional contributions to that evidence: First, this effect was associated to the presence of neglect, being absent in the group of patients without neglect. Second, replicating the results of Farah et al. [14], this ‘neglect-type’ deficit was as well present (though somewhat smaller) after auditory cues. The response delay in neglect patients corresponded to a higher number of misses for left vs. right targets. Remarkably, the size of this difference was negatively correlated with the BIT score, suggesting that the ‘neglect-type pattern’ reflects behavioural neglect.
4. The patients’ delay to invalidly cued left targets was more than the sum of the previous three factors. This was statistically corroborated by the significant interaction term of cue validity and target side. Thus, the ‘extinction-type pattern’ first reported by Posner et al. and replicated many times continued to be present after statistical removal of those other effects. Of interest, for response times this effect was only marginally significant in patients with neglect and, of much interest, this effect was not smaller (and statistically even more reliable) in patients without neglect than in patients with neglect. In terms of missing responses, the effect was clearly significant in patients with neglect and was markedly larger in patients with neglect than without. This classical ‘extinction-type’ effect on missing responses might reflect the ‘extinguished’ targets better than response delays, in agreement with competitive activation models or ‘race’ models of visual extinction.

We conclude that three pathological effects are reflected by

response times in the cue–target task: the general delay, the ‘neglect-type’ delay to all left-side stimuli, and the ‘extinction-type’ delay to invalidly cued left-side stimuli. The former two effects are associated to severity of clinical neglect, whereas the ‘extinction-type’ delay is a feature of patients with and without neglect.

The present data are certainly not decisive about the issue whether neglect and extinction are different pathological entities. First, as mentioned in Section 1, it may be questioned whether the extinction-type delay in this task is identical to other instances of extinction, as studied in bed-side testing. Of more importance, independence of the two effects in the present analyses does not imply independence of the two syndromes. It might well be that the extinction-type effect reflects a stable core symptom of neglect, remaining even after more severe pathology, indicated by the target-side effect, has gone.

As a methodological note, we were lucky to replicate the findings made in the cue–target task without presenting catch trials (i.e. trials where no targets are presented) and without varying the cue–target interval. Our procedure entailed the risk that participants would respond to cues rather than to targets. But the clear effects of target side and of cue validity, well corresponding to previous studies, are reassuring that participants followed instructions and indeed responded to targets.

A propensity of neglect patients to move their eyes ipsilaterally (i.e. to the right) is an unlikely explanation of the present results. This is suggested by a recent study of saccades in patients with right temporo-parietal lesions (some of them with neglect) performing a Posner task [40]. Patients made saccades more frequently than healthy controls, with a slight preference for rightward saccades which, however, was statistically not significant. About 65% of these saccades were directed to the target and not to the cue, even in the right cue–left target condition. In both conditions with invalid cues, these patients responded more slowly whenever they made a leftward (not rightward!) saccade. That study [40] concluded that the effort to perform a saccade into the left neglected hemifield causes an extra delay of manual response times. Thus, saccades may have contributed to the delayed response to left targets in our patients, but do not explain the extinction-type response pattern.

4.2. *Effects of auditory stimuli*

Auditory stimuli that replaced the visual stimuli as cues or targets had no or weak side-specific effects. This is in contrast to our expectations and, with respect to the lacking effects of side of auditory cues, in contrast to the results reported by Farah et al. [14].

One might suspect that the lacking effect of validity of auditory cues (in AC/VT) is precisely due to the methodological problem just mentioned, i.e. participants might have already triggered their responses in reaction to the

cues rather than to the targets. But this does obviously not apply to the neglect patients because there were still large effects of target side on these patients' responses in AC/VT. By inference, it does also not apply to the other groups. This inference is supported by the fact that the general differences in response times between groups remained the same between all three tasks. One argument in support of this suspicion is that responses were generally faster in AC/VT than in VC/VT, by about 100 ms. However, the same result was obtained by Farah et al. [14] who did include catch trials. The faster responses after auditory cues are probably due to the arousing effect of auditory stimuli as warning signals.

Another possibility why the side of auditory stimuli might have had so little effect is that these sounds could not be localised in space as easily as the visual stimuli. Easy left-right discrimination was the reason to use earphones (see Section 2 and Ref. [23]), and according to Simon [33] unilateral auditory stimulation by earphones induces an ipsilateral advantage of manual response times (Further discussion of this point follows below, in the context of methodological differences between the studies by Farah et al. [14] and the present one).

A more interesting possibility is that the sounds caused instantaneous arousal and that this arousal alleviated patients' deficits (see Ref. [31]), both the extinction-type pattern and the neglect-type pattern. In this line, the arousal caused by auditory cues would have abolished the extinction-type pattern, i.e. the effect of cue validity that would otherwise have been caused by these cues. Furthermore, arousal would have slightly reduced the neglect-type pattern, i.e. the side effect of visual targets that was slightly smaller in AC/VT than in VC/VT. When targets were auditory, in turn, in VC/AT, the arousal caused by auditory targets would have removed any validity effect of the visual cues (extinction-type pattern) as well as any effect of side of the auditory targets (neglect-type pattern). Interesting as this alternative may be, it appears implausible that arousal worked so perfectly, removing any side-specific effects of the very same stimuli that caused arousal.

A fourth alternative is that side of auditory stimuli does not interact with side of visual stimuli because space was not coded in a supramodal manner in this task. While this is the alternative that is theoretically most interesting, it is certainly not convincing at present, due to the presence of the alternatives just discussed, even though none of those alternatives was able to give a plausible account of the data pattern.

Whatever account is true, there is also the problem that the present results differ from the results reported by Farah et al. [14] where auditory cues did provoke the extinction-type pattern to visual targets, such that those authors concluded that space was coded in a supramodal manner.

Several differences between the studies might be responsible for these different outcomes. One difference is that in

their study the extinction-type effect was very large (see review of effects in Table 4 of Verleger et al. [40]) also for visual cues: With a cue–target interval of 150 ms (as used in the present study), the difference between invalidly and validly cued left targets amounted to 300 ms after visual cues, which is about three times larger than in the present data. After auditory cues, this difference reduced to 50 ms, which is about one sixth of the visual effect. Reducing the present VC/VT effect of 100 ms to one sixth its size would yield an effect of 16 ms only, which might be not reliable. Therefore, in any case, both studies agree that with a 150 ms cue–target interval the extinction-type pattern is much smaller after auditory than after visual cues. Perhaps, therefore, the difference between the conclusions of the two studies is more apparent than real.

Assuming that the results do differ between the two studies, methodological differences might be responsible. One important difference is that free-field loudspeakers were used in the Farah et al. study [14] rather than earphones. Thus, sounds probably were less well localisable and less intrusive in their study. Both features do not account for the presence of a differential effect of side in their data, on the contrary. However, free-field sounds might be less arousing than sounds played directly to the ear. Thus, there might have been less compensation by the arousing property of sounds in their study.

Theoretically even more interesting is a possible consequence of the fact that the loudspeakers were placed nearby the visual stimuli in the study by Farah et al. Perhaps, this neighbourhood of sounds and visual stimuli was needed to bind their spatial codes together, interpreted by the localising system as features of common objects in extrapersonal space [15]. Cross-modal perceptual integration has been shown to require spatial alignment of stimuli [22]. In contrast, sounds played to the left or right ear by earphones are perceived as proximal stimuli in personal space, providing just the abstract code 'left' and 'right'.

Thus, as the extinction-type deficit was found to be essentially limited to the visual domain, our data do not contain evidence that spatial coding proceeds in a supramodal manner. However, according to the literature, such supramodal processing might occur if there is spatial alignment of visual auditory stimuli such that they can be interpreted as features of common objects.

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