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Left visual neglect: Is the disengage deficit space- or object-based?

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Abstract

Attention can be directed to spatial locations or to objects in space. Patients with left unilateral spatial neglect are slowed to respond to a left-sided target when it is preceded by a right-sided “invalid” cue, particularly at short cue-target intervals, suggesting an impairment in disengaging attention from the right side in order to orient it leftward. We wondered whether this deficit is purely spatial, or it is influenced by the presence of a right-sided visual object. To answer this question, we tested 10 right brain-damaged patients with chronic left neglect and 41 control participants on a cued response time (RT) detection task in which targets could appear in either of two lateral boxes. In different conditions, non-informative peripheral cues either consisted in the brightening of the contour of one lateral box (onset cue condition), or in the complete disappearance of one lateral box (offset cue condition). The target followed the cue at different stimulus-onset asynchronies (SOAs). If the disengagement deficit is purely space-based, then it should not vary across the two cueing conditions. With onset cues patients showed a typical disengagement deficit at short SOAs. With offset cues, however, the disengagement deficit disappeared. Thus, patients did not show any disengagement deficit when there was no object from which attention must be disengaged. These findings indicate that the attentional bias in left neglect does not concern spatial locations per se, but visual objects in space.

Key words: Spatial Attention, Brain Damage, Response Time

Introduction

Patients with right brain damage and visual neglect fail to orient and respond to left-sided visual stimuli. A large amount of neuropsychological evidence suggests that neglect is a heterogeneous syndrome (Bartolomeo 2007), but some of its underlying mechanisms may be understood as an association of disorders of visual attention (Bartolomeo and Chokron 2002).

For example, Posner and his colleagues (Posner et al. 1984; Posner et al. 1987) have proposed an influential model of attentional disorders in neglect/extinction. In Posner et al.'s framework, at least three operations are involved in normal attentional orienting (Posner 1980): First, attention is disengaged from its actual focus of fixation; then it is moved towards the target location, and finally there is a new engagement at the target location. This hypothesis was based on evidence from a speeded visual detection visual orienting paradigm (Posner 1980). In this paradigm, following a central (e.g. a left- or right-pointing arrow) or a peripheral cue (e.g. a luminance increase in one of the possible target locations), a target appears either at the cued location (i.e. valid cue condition) or at an uncued location (i.e. invalid cue condition). Normal individuals usually show an advantage for valid trials as compared to invalid ones (the facilitation effect). This suggests that the cue prompts attention to be oriented towards the cued location, which speeds up processing of targets appearing at that region and slows down responses to targets appearing at other locations. When a target is presented at a cued location, attention is already engaged at this location, which results in quick responses. In contrast, when the cue and the target appear at different locations (invalid trials), attention must be disengaged from the wrong location, moved towards the actual target location and then engaged on the target. These additional steps would be responsible for the delay in response times (RTs) observed on invalid trials. Facilitation effects can be found with both central symbolic cues signalling the most likely target location (known as endogenous

cues), and with peripheral, abrupt onset cues, that may not predict the target location (known as exogenous cues). This result is consistent with the view that there are two modes by which attention can be oriented; a voluntary or *endogenous mode*, which is responsive to internally developed expectancies, and a reflexive or *exogenous mode*, which is related to the perceptual saliency of external stimuli. Endogenous orienting is long lasting, whereas exogenous attentional orienting quickly disappears, leading to a reversion in the effect at longer cue-target Stimulus Onset Asynchronies (SOA), i.e., slower RTs on valid trials. This phenomenon is often labelled Inhibition of Return (IOR; Posner et al. 1985), and its mechanisms are currently object of intense debate (Bartolomeo and Lupiáñez 2006). Using the cued detection paradigm, Posner and co-workers (Posner et al. 1984; Posner et al. 1987) reported that patients with parietal lobe damage exhibit disproportionately slow RTs to contralesional targets preceded by ipsilesional cues, and interpreted this pattern of results as reflecting a difficulty in disengaging attention from an invalidly precued location in the ipsilesional hemifield when the target is presented in the contralesional field. This “disengagement deficit” (DD) can be observed after damage to either hemisphere (Posner et al. 1984), and in patients with or without signs of spatial neglect (Posner et al. 1984; Friedrich et al. 1998; Siéhoff et al. 2007). However, the DD is particularly evident after right hemisphere lesions, with peripheral cues, with short SOAs, and in patients with left neglect (Morrow and Ratcliff 1988; Losier and Klein 2001; Bartolomeo and Chokron 2002; Siéhoff et al. 2007). Taken together, these features suggest an impairment in exogenous orienting towards targets in contralesional space as an important component deficit of left visual neglect (Smania et al. 1998; Bartolomeo et al. 2001; Siéhoff et al. 2007). In contrast, endogenous orienting seem to be relatively preserved, if slowed, in left unilateral neglect (Smania et al. 1998; Bartolomeo et al. 2001).

This response delay to contralateral stimuli preceded by ipsilateral exogenous cues appears to be a stable marker of neglect. Indeed, even if the DD is greater in neglect patients

with right hemisphere damage, it is also present in patients with left brain damage, but only if they show signs of right neglect (Losier and Klein 2001). Therefore, a causal relationship between the magnitude of the DD and the severity of neglect has been suggested (Morrow and Ratcliff 1988; but see Siéoff et al. 2007), despite the fact that DD can also be observed in patients without clinical signs of neglect (Posner et al. 1984). Thus, the DD can be a valuable marker for clinical assessment of neglect patients, for example in evaluating the therapeutic effect of rehabilitation strategies (Striemer and Danckert 2007).

The DD was originally conceived as a difficulty in disengaging attention “from a location other than the target” (Posner et al. 1984, p. 1872). However, attention can be directed not only to a region of space, but also (and perhaps more importantly) to visual objects in space (Egley et al. 1994; Valdes-Sosa et al. 1998). This raises important issues concerning of the nature of the DD. Does the DD reflect a directional deficit of disengaging attention from an ipsilesional to a contralesional location (Posner et al. 1987), or could it better be conceived as an impaired disengagement from visual *objects* presented on the ipsilesional side?

To address this issue, we asked normal controls and neglect patients to perform a speeded detection task in which targets were preceded by non-informative peripheral cues. In one condition, the cue consisted on the brightening of one of two lateral boxes (onset cues), whereas in the other condition the cue consisted on the disappearance of one box (offset cues). It has been shown that both types of cue can attract spatial attention and produce standard facilitation effects at short SOAs (Pratt and McAuliffe 2001). Therefore, if neglect patients' DD is exclusively space-based, it should occur even with offset cues. If, on the contrary, the DD concerns not space per se, but objects in space, then the DD should occur only in, or be increased by, the onset condition.

A further issue of interest concerns the question of how onset and offset cues influence the IOR phenomenon. Among the several controversies concerning the nature and mechanisms of IOR (see Bartolomeo and Lupiáñez 2006), it has been suggested that right brain-damaged patients can show asymmetric IOR, which may decrease (Vivas et al. 2006) or even revert to facilitation on the ipsilesional side (Bartolomeo et al. 1999). If abnormal IOR depends only on the side of presentation, then it should not vary with the nature of the cue (onset or offset). If, on the other hand, abnormal IOR on the right side results from the abnormal persistence of attention on right-sided cues, then the abnormal advantage for cued trials should be increased in the onset condition.

Method

Participants

Ten patients with right unilateral hemispheric lesions and chronic left neglect and 41 participants without neurological impairment consented to participate in the study, which was carried out by following the guidelines of the Ethics Committee of the Salpêtrière Hospital in Paris. Patients were included on the basis of showing signs of left visual neglect, as assessed by means of tests of letter and shape cancellation and line bisection (see Bartolomeo and Chokron 1999, for a detailed description of the tests). All participants were right-handed and reported normal or corrected-to-normal vision. No patient had hemianopia (which was an exclusion criterion), but 4 showed visual extinction for left targets on double simultaneous visual stimulation. Patients' mean age was 65.3 years (SD, 11.58; range, 41-81). Control participants was divided in two subgroups, an "old" control group (N=15; mean age, 66.4 years; SD, 12.63; range, 49-87), which matched in age the patient group, and a "young" control group (N=26; mean age, 28.8 years; SD, 4.1; range, 23-37), in order to explore

possible age-based differences in performance. Table 1 shows the demographic and clinical characteristics of patients, as well as their performance on the neglect battery.

-----Insert table 1 about here-----

Apparatus and stimuli

Stimulus presentation and response collection were controlled by SuperLab Pro (version 2.0.4; www.superlab.com). Three empty black square boxes, with a 1.4° long, 0.5° thick side, were displayed on a white background. The boxes were horizontally arranged, with the central box being located at the center of the screen. The central box contained a small rectangular black fixation point ($0.15^\circ \times 0.2^\circ$). Distance between boxes was 4.1° . In different tests, cues either consisted in the thickening of the contour of one lateral box (from 0.1° to 0.2° ; hereafter "onset" cues), or in the disappearance of one lateral box ("offset" cues). Cues remained on or off until the end of each trial. The target was an asterisk 0.6° wide appearing inside one of the lateral boxes, at a retinal eccentricity of about 4.8° . The target followed the cue at 100, 500, or 1,000-ms SOA. Targets appeared with equal probabilities at the cued or at the uncued location, thus cues were not informative about target location.

Procedure

Participants sat in front of a computer monitor at a distance of approximately 57 cm. Each trial began with the appearance of the three boxes for 500 ms. After that time the cue appeared in one of the two peripheral boxes. Then the target appeared and remained visible for 5 seconds or until a response was made. After an intertrial interval of 1,000 ms, a new trial began. Participants were asked to respond to the target as soon as possible, by pressing the space bar of the computer keyboard. Two different cue-target combinations were presented in each recording run. In the valid condition the cue correctly indicated the position of the target. In the invalid condition the cue appeared or disappeared at the lateral box opposite the

location of the subsequent target. These cue conditions were equiprobable and the targets appeared equally to the left and right of fixation. Each participant received 12 practice trials followed by 192 trials intermingled randomly within two blocks. A brief period of rest was allowed between blocks. The onset and offset tests were blocked, and administered in counterbalanced order across participants.

Participants were instructed to maintain fixation and to respond to the target as quickly and accurately as possible, by pressing the space bar on a standard keyboard with their right index finger. Participants were told that the side of appearance of the cue was not informative about the side of the upcoming target, and were instructed to respond exclusively to the targets. Eye movements were controlled by one of the experimenters, who sat in front of the participants during the practice block and if a saccade took place, gave feedback to the participants together with further instructions to fix the central cross on the remaining trials. Patients unable to maintain fixation throughout the remaining practice trials were excluded from the study. The procedure is summarized graphically in Figure 1.

-----Insert Fig. 1 about here-----

Results

Patients who were unable to maintain the fixation or who had no signs of neglect at the time of test were excluded from analysis. This led to the exclusion of 24 patients out of the 34 originally recruited. Trials with RTs slower or greater than 2.5 SD per participant per side were eliminated from the analysis (2.6% of trials on average; range, 0.56% - 5.29%). Mean RTs were computed for each experimental condition (Table 2) and introduced in a repeated-measures analysis of variance (ANOVA) with the following factors: *Group* (Young Controls, Old Controls and Neglect Patients), *Test* (On, Off), *Side* (Left, Right), *SOA* (100, 500, 1,000

ms) and *Cueing* (Cued, Uncued). The Group variable was manipulated between participants, whereas the other variables were manipulated within participants. The α level was set to 0.05.

-----Insert Table 2 about here-----

Neglect patients were much slower than controls, $F(2, 48)=37.806$, $p < 0.0001$, especially for left targets (Group x Side interaction, $F(2, 48)=16.454$, $p < 0.0001$). Given this substantial difference in mean RTs, and in order to be able to compare the size of the effects shown by neglect patients to that of the control groups, a further ANOVA was performed with the same factors on the proportional RTs, i.e. the RT on each specific experimental condition per participant, divided by the average RT for that participant (see Lupiáñez et al. 2004).

The interaction between the five factors was significant ($F(4, 96)=3.95$, $p = 0.006$). To explore this complex pattern of interaction, and following our a priori predictions, we performed four different Group x Side x Cueing ANOVAs, two on the data from the short, 100-ms SOA (one for the On Test, and the other for the Off Test), where facilitation is predicted, and two on the data from the longest, 1,000-ms SOA, where IOR is predicted instead.

The Side x Group interaction was significant in all cases, showing the already described pattern (neglect patients' longer RTs for left-sided targets than for right-sided targets), and will no longer be reported.

The ANOVA performed on the *short SOA, On Test* condition revealed a significant three way interaction, $F(2, 48)=9.5257$, $p < 0.001$, resulting from a substantial slowing in neglect patients for uncued left targets, i.e. a typical DD (Fig. 2A).

-----Insert Fig. 2 about here-----

This cueing effect for left-sided targets was significantly larger than that for right-sided targets in neglect patients, $F(1, 9)=7.978$, $p = 0.0199$, as well as than that for left-sided target

in the two groups of controls, $F(2, 49)=11.505$, $p < 0.0001$, which did not differ between each other $F < 1$.

In contrast, the ANOVA performed on the *short SOA, Off Test* condition (Fig. 2B) showed a highly significant Cueing effect, $F(1, 48)=15.529$, $p = 0.0003$, which was independent of Side and Group (all $ps > 0.12$).

-----Insert Fig. 3 about here-----

Turning now to the 1,000-ms *long SOA*, the ANOVA performed on the *On Test* condition showed again a significant interaction between cueing and Group, $F(2, 48)=4.715$, $p = 0.014$ (Fig. 3A). However, in this case the interaction was independent of side, $F < 1$, and resulted from the opposite cueing effect shown by old and young controls, $F(1, 39)=13.652$, $p = 0.0007$. In support of this interpretation, the interaction between cue and group resulted far from significance when the controls were analyzed as a single group without age differentiation ($F < 1$). Interestingly, whereas young controls showed an IOR effect (slower RT for cued than for uncued trials), which just failed to reach significance, $F(1, 25)=4.041$, $p = 0.055$, old controls showed significant facilitation (faster RT for cued than for uncued trials, $F(1, 14)=9.157$, $p = 0.0091$). Neglect patients showed no significant effect at all, although the tendency was to show IOR for left targets and facilitation for right targets (both $Fs < 1$), consistent with previous reports (Bartolomeo et al. 1999; Vivas et al. 2006).

The ANOVA performed on the data from the *long SOA, Off Test* condition showed a significantly larger cueing effect for neglect patients than for controls, $F(2, 48)=5.442$, $p = 0.0074$. However, in this case the effect was independent of side, $F < 1$ (Fig. 4B), and therefore it cannot be interpreted as reflecting a DD.

Discussion

Attention is a heterogeneous set of processes whose aim is to maintain coherent behavior in the face of irrelevant distractions, while allowing the agent to respond rapidly to novel and

important stimuli. Brain damage can severely disrupt these processes. For example, neglect patients' attention can be captured by ipsilesional stimuli (Gainotti et al. 1991; D'Erme et al. 1992; Bartolomeo et al. 2004), even if they are irrelevant to the current task. After ipsilesional capture, patients' attention may remain, as it were, "stuck" on non-neglected items, so that its reorienting to other portions of the visual space is slowed (DD). The aim of the present study was to determine whether the locus of the DD is purely spatial, as it is commonly assumed, or whether visual objects in space are in fact crucial to capture and confine patients' attention.

Concerning this issue, our results in neglect patients are clear-cut. A typical DD was obtained with onset cues at short SOA, but the DD completely disappeared with offset cues. Except for the overall slowed RTs, neglect patients demonstrated a similar pattern of results as both young and old controls in the offset condition at short SOA. Thus, in the absence of a visual stimulus capable of holding their attention on the non-neglected side, neglect patients are able to redirect attention to the neglected side in a relatively fast manner.

Previous studies using paper-and-pencil tasks have provided abundant analogous evidence of normal or near-normal performance in neglect patients in the absence of attention-capturing stimuli on the right side. For example, neglect patients performance can improve when visual feedback is minimal or absent (Chokron et al. 2004; Loetscher and Brugger 2007; Urbanski and Bartolomeo 2008). When patients had to detect multiple targets on a paper sheet, either by drawing over them with a pencil stroke or by erasing them, they omitted more left-sided target in the "draw" than in the "erase" condition, as if the already detected right-sided targets continued to capture their attention when still present on the sheet (Mark et al. 1988; see also Làdavas et al. 1993). Even when the right-sided objects are not targets, but distractors, they can nevertheless exacerbate neglect-related behaviour (Bartolomeo et al. 2004). Finally, more relevant to the present context, in a Posner-like RT task patients demonstrated more DD when the targets appeared in placeholder boxes than

when they appeared in a blank space (D'Erme et al. 1992). D'Erme et al interpreted their findings as suggesting that right-sided box exogenously captured patients' attention and kept it confined. The present results directly support this interpretation. The privileged status of stimulus onsets, as compared to stimulus offsets, to capture and maintain attention is also consistent with evidence from visual search tasks in normal participants (see, e.g. Yantis and Jonides 1990).

In a study devoted to discriminate space-based from object-based neglect, Behrmann and Tipper (1999) asked left neglect patients to respond to targets appearing inside one of two horizontally aligned circles of different colors. As expected, patients responded faster to right than to left targets (space-based neglect). However, in most (~80%) patients this effect was reversed when the two circles were connected by a line, like a barbell (thus forming a single perceptual object), and the barbell rotated by 180° just before the target appeared. In this case, RTs for the targets now on the left side, but appearing in a previously right-sided circle, were faster than RTs for the targets appearing on the right, thus suggesting object-based neglect. A possible account of these results is that the circle originally on the right side captured patients' attention and generated a cost (DD) for targets appearing on the left-sided circle. Patients' attention then followed the circle as it changed its location. Thus, neglect was not only modulated by the absolute spatial location of the target, but also by the target being an object capable of holding attention "stuck". On the other hand, when the two circles were treated as a single object, the right side of space by itself was insufficient to retain patients' attention and to generate a DD, in agreement with the present results.

However, in our results the confinement of attention to the attended objects disappeared with time. Thus, at long SOA, the strong DD demonstrated by neglect patients with onset cues disappeared. This dependency of DD on SOA has repeatedly been reported in the literature (see Losier and Klein 2001, for review), and is also consistent with the

prevalently exogenous nature of the attentional bias in neglect, because, as already mentioned, exogenous orienting typically occurs at short SOAs (Müller and Rabbitt 1989).

A general caveat in interpreting the present results at long SOA is that we cannot completely rule out the possibility of contamination from occasional eye movements. Despite the fact that all participants were able to maintain fixation and complied with the instructions, with long SOA we cannot exclude the possibility that eye movements occurred in occasional trials and went undetected by the examiner. Thus, while the lack of IOR for right-sided targets in neglect patients with the onset test confirmed previous similar results (Bartolomeo et al. 1999; Vivas et al. 2006), we cannot exclude that an advantage for cued trials might have resulted from patients occasionally looking a right-sided cues, and consequently receiving the target at the fovea.

A similar caveat applies to the results shown by control participants, who showed an intriguing pattern of performance with the onset test at long SOA. While young controls showed a marginally significant IOR, old controls had significant facilitation. Despite the possibility of eye movements, we note that this pattern is in agreement with previous reports in the literature showing a lack of IOR in older adults (Faust and Balota 1997). The fact that no cue back was presented between the cue and the target (see Posner and Cohen 1984), and the presence of a temporal overlap between cues and targets might explain why IOR was only marginally significant for young controls, and completely absent for old controls, who demonstrated instead significant facilitation. However, this pattern was not observed with offset cues, where controls showed no difference between cued and uncued trials. The discrepancy between onset and offset cues might suggest that these cueing effects are related to object (cue-target) integration processes. It has indeed been proposed that IOR might be due to the lack of novelty induced by an old object (i.e., the cue) in the processing of the target when it appears in the same location, leading the system to treat the target as less novel,

and thus less able to capture attention (Lupiáñez et al. 2007). Note that this tendency to integrate the target within the object file of the cue might be clearly reduced or eliminated when the cue disappears, as in the off condition. Contrary to this hypothesis, previous studies (e.g., Riggio et al. 1998) did demonstrate IOR with offset cues. However, in these previous studies a visual object (the placeholder box) remained in the location signalled by the offset cue, and the target appeared inside the box. In the present case, instead, the cue offset consisted in the disappearance of the box, leaving a blank location on the screen. Thus, in the present experiment the perceptual discrimination between off cues and targets was probably much easier.

An unexpected finding was the large facilitation for cued trials in the offset test for neglect patients at long SOA. Although we cannot offer a plausible explanation for this effect, we note that it was clearly independent of side, and therefore must be considered as different from standard DD.

In conclusion, the present results demonstrate an important characteristic of the disengagement deficit in neglect patients: The presence of a visual object in which the target appears is a necessary condition for the DD to emerge. As a consequence, the DD cannot simply be considered as a directional spatial deficit (Posner et al. 1987). Any future models of orienting of attention in neglect must take into account the relationship of the DD to visual objects in space.

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Tables

Table 1. Demographical and clinical characteristics of neglect patients

<i>Patient</i>	<i>Sex / age / years of schooling</i>	<i>Months since onset</i>	<i>Aetiology</i>	<i>Locus of lesion</i>	<i>Bells cancellation (number of left/right hits, max 15/15)</i>	<i>Letter cancellation (number of left/right hits, max 30/30)</i>	<i>Line bisection (% deviation)</i>
1	M / 73 / 10	7	Ischemic	P, O	12 / 14	23 / 27	+5.71
2	M / 41 / 10	2	Hemorrhagic	P, T	13 / 13	7 / 25	+29.05
3	M / 55 / 12	3	Hemorrhagic	P, T	7 / 12	27 / 29	+9.05
4	M / 59 / 8	17	Ischemic + Hemorrhagic	IC, BG	14 / 15	14 / 17	+6.43
5	M / 81 / 16	2	Ischemic + Hemorrhagic	O	15 / 14	26 / 28	+38.81
6	F / 64 / 10	8	Hemorrhagic	F, P, T,	0 / 11	6 / 27	+11.38
7	M / 76 / 8	3	Ischemic	F, P, T,	0 / 5	24 / 27	+9.28
8	M / 67 / 12	2	Ischemic + Hemorrhagic	F, P, T, BG	12 / 15	23 / 29	+8.9
9	M / 72 / 16	7	Ischemic	F, P, T,	13 / 15	28 / 30	+6.51
10	M / 65 / 16	9	Ischemic	T, I, BG	8 / 15	28 / 30	-0.5

See Bartolomeo and Chokron (1999) for detailed test description. For the line bisection test, the cumulated percentage of deviation from the true centre of all the lines was calculated, with rightward deviations carrying a positive sign and leftward deviations having a negative sign. For the cancellation tests, the number of items cancelled on the left / right halves of the page is reported. Locus of lesion: P, parietal; O, occipital; T, temporal; F, frontal; IC, internal capsule; BG, basal ganglia; I, insula.

Table 2. Mean RTs per experimental condition.

Group	Cue Type	Cueing	Left Side			Right Side		
			100 ms	500ms	1000 ms	100 ms	500ms	1000 ms
Neglect	Off	Uncued	1005	1081	1075	761	741	814
		Cued	967	1011	915	722	691	741
		Cueing Effect	38	70	160	39	51	99
	On	Uncued	1122	1004	875	781	836	740
		Cued	883	985	948	722	677	712
		Cueing Effect	239	19	-73	58	159	28
Young Controls	Off	Uncued	410	381	371	402	380	361
		Cued	393	381	373	397	381	367
		Cueing Effect	17	0	-2	5	-1	-5
	On	Uncued	432	380	371	435	392	373
		Cued	406	402	385	405	394	377
		Cueing Effect	26	-21	-13	29	-2	-4
Old Controls	Off	Uncued	530	503	485	517	497	477
		Cued	499	478	485	498	467	483
		Cueing Effect	31	25	1	19	30	-7
	On	Uncued	584	556	523	582	533	518
		Cued	541	506	493	527	511	490
		Cueing Effect	43	50	30	55	22	28

Figure Legends

Figure 1. Outline of the experimental procedure depicting the sequence of events in each of the two experimental conditions. The onset cue test consisted in the brightening of the contour of one of the boxes, which remained present until the end of the trial. The offset cue test consisted on the disappearance of one of the lateral boxes, which remained absent until the end of the trial.

Figure 2: RTs for the onset test (A) and the offset test (B) at short (100-ms) SOA.

Figure 3: RTs for the onset test (A) and the offset test (B) at long (1,000-ms) SOA.

Fig. 1

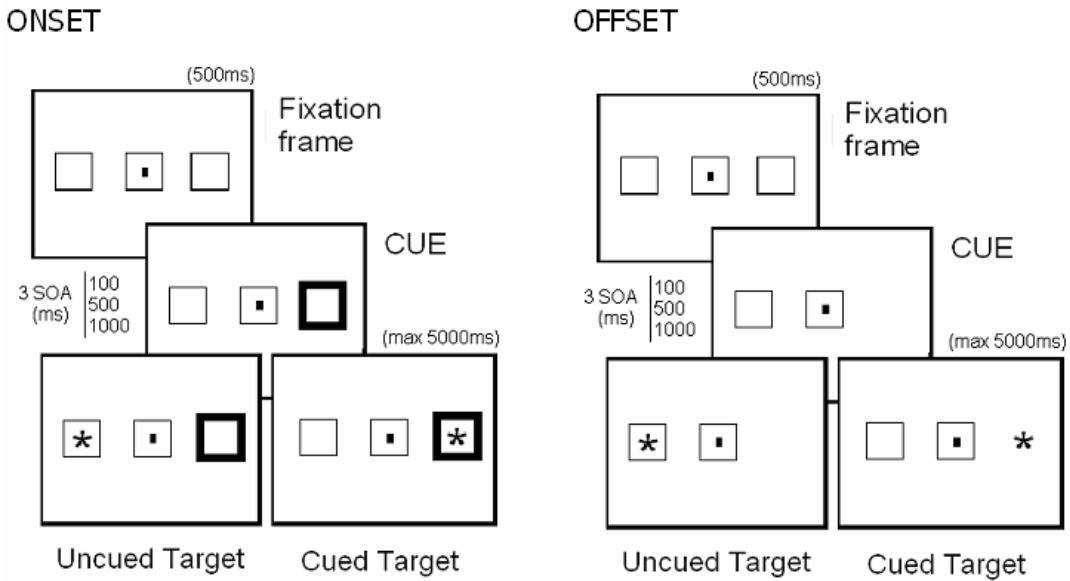


Fig. 2

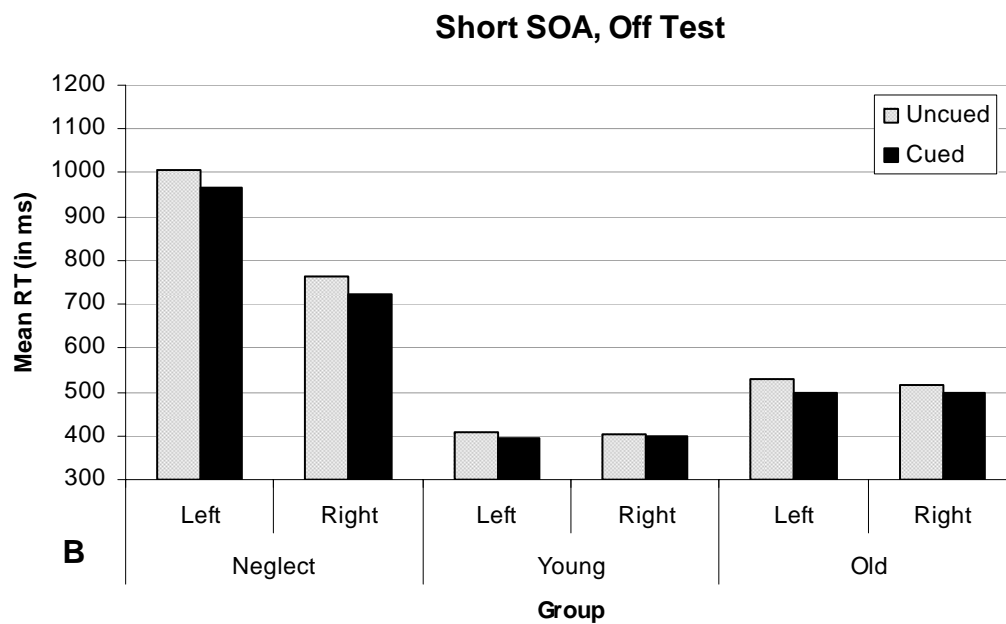
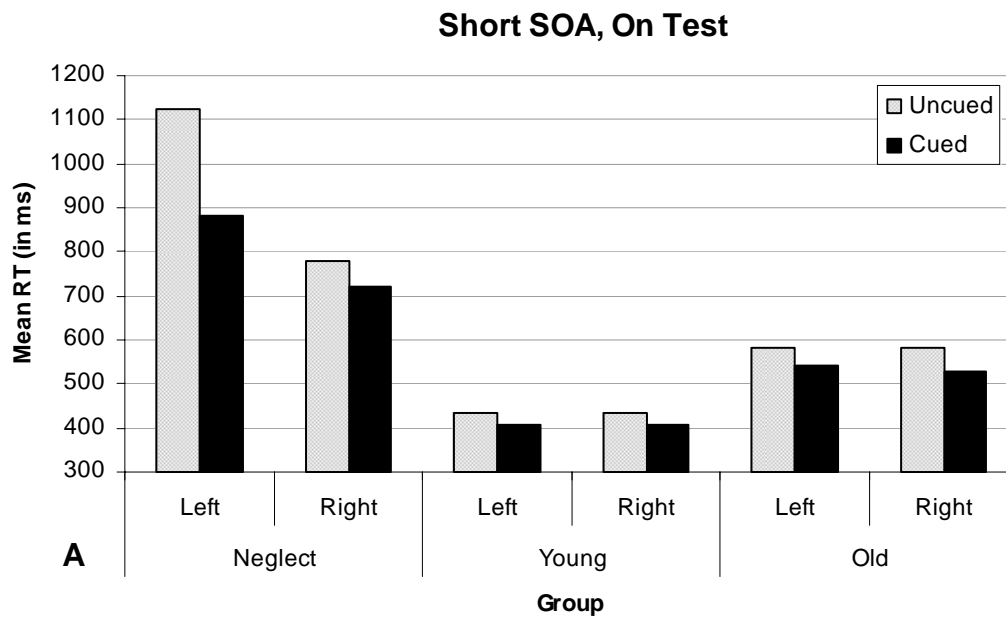


Fig. 3

