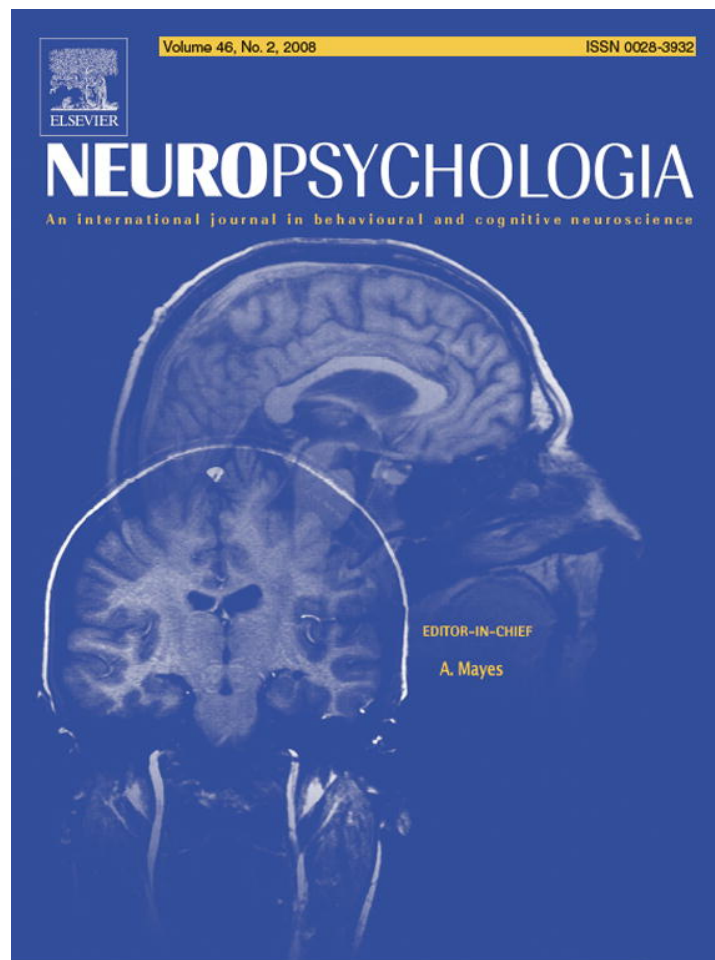


Provided for non-commercial research and education use.
Not for reproduction, distribution or commercial use.



This article was published in an Elsevier journal. The attached copy is furnished to the author for non-commercial research and education use, including for instruction at the author's institution, sharing with colleagues and providing to institution administration.

Other uses, including reproduction and distribution, or selling or licensing copies, or posting to personal, institutional or third party websites are prohibited.

In most cases authors are permitted to post their version of the article (e.g. in Word or Tex form) to their personal website or institutional repository. Authors requiring further information regarding Elsevier's archiving and manuscript policies are encouraged to visit:

<http://www.elsevier.com/copyright>



ELSEVIER

Neuropsychologia 46 (2008) 426–433

www.elsevier.com/locate/neuropsychologia

NEUROPSYCHOLOGIA

Modulation of hemispatial neglect by directional and numerical cues in the line bisection task

Mario Bonato^a, Konstantinos Piftis^{a,b}, Roberto Marenzi^c, Marco Zorzi^{a,*}

^a University of Padova, Italy

^b IRCCS San Camillo, Lido-Venezia, Italy

^c Centro di Riabilitazione di Conselve, Azienda Ospedaliera di Padova, Padova, Italy

Received 9 May 2007; received in revised form 24 July 2007; accepted 24 August 2007

Available online 31 August 2007

Abstract

We investigated the effects of arrows, eye gaze, and digits presented as irrelevant flankers in a line bisection task that was administered to 17 right brain damaged patients with or without left neglect. The rightward bias of neglect patients was selectively modulated by the direction of eye gaze and by the magnitude of two identical digits. The bisection error was shifted contralesionally by leftward-gazing eyes and “small” digits, whereas it was shifted ipsilesionally by rightward-gazing eyes and “large” digits. Therefore, the performance of neglect patients was influenced by task-irrelevant cues whose directional meaning was either explicitly represented (eye gaze) or related to the activation of a spatially oriented mental representation (digits). Regression analyses of the overall performance revealed that size of the rightward bias and error variability were predicted by neglect assessment scores across the entire sample of right brain damaged patients. The increased variability in line bisection performance is consistent with the “indifference zone” theory and it appears to be a subtle but stable marker of neglect.

© 2007 Elsevier Ltd. All rights reserved.

Keywords: Neglect; Line bisection; Number processing; Eye gaze; Arrows

Neglect is an acquired multicomponential neuropsychological syndrome characterised by the impairment of conscious processing of stimuli in the contralesional hemispace (Halligan, Fink, Marshall, & Vallar, 2003; Parton, Malhotra, & Husain, 2004). Neglect has been described more frequently after damage to the right inferior parietal lobule or to the right temporoparietal junction and, consequently, the neglected hemispace is usually the left (Vallar, 2001).

The line bisection task is one of the most common clinical tests employed to assess neglect. It consists in marking the mid-point of a visually presented line (Bisiach, Capitani, Colombo, & Spinnler, 1976; Schenkenberg, Bradford, & Ajax, 1980). Neglect patients typically shift their subjective midpoint towards the ipsilesional hemispace as if they were not aware of the contralesional end of the line. Healthy participants, in contrast, show “pseudoneglect” that is a mild leftwards bias with

respect to the true midpoint of the line (for a review see Jewell & McCourt, 2000).

The line bisection task can be “cued” in different ways (see Fischer, 2001a, for review). The first studies in the field employed relevant cueing (Nichelli, Rinaldi, & Cubelli, 1989; Riddoch & Humphreys, 1983). The aim of these studies was to assess whether shifting voluntary attention towards the neglected hemispace would have ameliorated bisection performance. Participants were usually required to read aloud a letter presented at one end (left vs. right) or at both ends of the to-be-bisected line. The rightward shift of neglect patients, observed in the uncued condition, decreased following left cueing, that is when bisection was performed after reading the letter placed on the left (Riddoch & Humphreys, 1983; but see also Heilman & Valenstein, 1979). A second cueing modality is to use cues that have a directional meaning. The most straightforward type of directional cue is one that explicitly represents a spatial orientation, such as pointing arrows or gazing eyes. Reaction time studies of healthy participants have shown that these cues automatically generate a spatial code (e.g., Zorzi, Mapelli, Rusconi, & Umiltà, 2003) and trigger reflexive shifts of spatial attention (e.g., Driver et al., 1999; Friesen & Kingstone, 1998; Gibson & Kingstone,

* Corresponding author at: Dipartimento di Psicologia Generale, University of Padova, via Venezia 8, 35131 Padova, Italy. Tel.: +39 049 8276618.

E-mail address: marco.zorzi@unipd.it (M. Zorzi).

URL: <http://ccnl.psy.unipd.it> (M. Zorzi).

2006; Ristic & Kingstone, 2006). Cueing by arrows was also employed in several studies of line bisection in healthy participants. The most common finding is that arrow cueing shifts the subjective midpoint towards the direction opposite to the orientation of the arrows (Chieffi, 1999; Kashmere & Kirk, 1997; Macdonald-Nethercott, Kinnear, & Venneri, 2000). To the best of our knowledge, direction of eye gaze has never been used to cue the line bisection task. However, one would predict that gaze cues can modulate neglect performance; indeed, Vuilleumier (2002) reported that the extinction rate of right brain-damaged patients was ameliorated when a left target was cued by leftward gazing eyes.

One further type of cue that conveys directional meaning is a one-digit number. Directional meaning is not explicit in this case but it is related to the activation of a spatial representation of numbers in the form of a left-to-right oriented mental number line (for reviews see Fias & Fischer, 2005; Hubbard, Piazza, Pinel, & Dehaene, 2005). Reaction time studies of healthy participants have shown the association between response side and numerical magnitude, in the form of a left-small versus right-large correspondence (the SNARC effect; Dehaene, Bossini, & Giraux, 1993). More direct evidence for the spatial coding of numbers has been reported by Zorzi, Priftis, and Umiltà (2002), who asked left neglect patients to mentally bisect numerical intervals (e.g., “What number is halfway between 1 and 9?”). Neglect patients reported a number larger than the correct one (e.g., “7”), shifting the response towards the “right” end of the mental number line (also see Priftis, Zorzi, Meneghello, Marenzi, & Umiltà, 2006; Zorzi, Priftis, Meneghello, Marenzi, & Umiltà, 2006). Finally, centrally presented digits produce lateral shifts of spatial attention that are related to their numerical magnitude (Casarotti, Michielin, Zorzi, & Umiltà, 2007; Fischer, Castel, Dodd, & Pratt, 2003) and can influence the execution of pointing movements (Ishihara et al., 2006).

The effect of digit cueing upon line bisection performance has been studied with healthy participants only. Fischer (2001b) first reported that the bisection of lines made up by a string of digits (e.g., 11111111) was modulated by numerical magnitude. Fischer found a rightward deviation for lines composed of “large” numbers (8 and 9) and a leftward deviation for lines composed of “small” numbers (1 and 2). In a second experiment, two different digits (1 and 2 or 8 and 9) were placed at the extremities of each line. Results revealed a shift towards the larger of the two digits, that had to be reported before bisecting the line. Calabria and Rossetti (2005) also presented lines composed of digits but they did not find a deviation of the midpoint as a function of number magnitude. Nonetheless, the effect was present when the line was made up by a continuous sequence of written number words (e.g., the French translation of NINENINENINENINE). Finally, de Hevia, Girelli and Vallar (2006) did not replicate the findings of Fischer (2001b) with lines made from digits, whereas they found a more consistent shift towards the numerically larger of two digits presented as flankers at the ends of to-be-bisected lines or empty spaces, and interpreted this finding as an illusion of length induced by the larger digit.

In the present study, we directly compared the effects of gazing eyes, arrows, and Arabic digits used as task-irrelevant

flankers in a line bisection task. The finding that these types of stimuli can influence spatial processing and produce shifts of attention in healthy participants leads to the question of whether they can modulate performance of neglect patients in the line bisection task. Notably, neglect patients seem to be more sensitive than brain damaged controls to task-relevant cues (e.g., Olk & Harvey, 2002) as well as to (task-irrelevant) illusions of length (e.g., Daini, Angelelli, Antonucci, Cappa, & Vallar, 2002). Thus, irrelevant visual cues might be particularly effective in the case of neglect patients. The use of different types of cue within the same patients allows us to compare the effect of social cues (eye gaze), symbolic cues (arrows), and numerical cues (digits). The directional meaning is explicitly represented in the case of eye gaze and arrows, whereas it is implicit in the case of digits (i.e., related to the activation of their mental representation). Both eye gaze and digits have not been used in previous studies of line bisection with neglect patients.

With regard to the effect of specific cues, the results of the studies reviewed above lead to the following set of predictions: (i) bisection error should be shifted towards the direction indicated by the gazing eyes; (ii) the effect of arrows should be very similar to that of gazing eyes, although the inconsistent results regarding arrow-cued line bisection in healthy participants do not allow us to use a directional hypothesis; (iii) small digits (i.e., 1-1) should shift the bisection error towards the contralesional hemispace, whereas the opposite shift should be observed for large digits (i.e., 9-9); (iv) two different digits placed at the ends of the line should induce a shift towards the larger number.

1. Method

1.1. Participants

Seventeen consecutive patients with right hemisphere lesion participated in the study. Patients were admitted to a rehabilitation centre for the treatment of their neuromotor deficits; patients' demographic, clinical, and neuropsychological data are reported in Table 1. None had a history of substance abuse or other neurological diseases. All participants gave written informed consent to take part in the study, according to the Declaration of Helsinki. The presence of a single right hemisphere lesion was confirmed by CT or MR scans. Participants were initially screened with the Mini Mental State Examination (Italian version of Magni et al., 1996) to exclude the presence of diffuse cognitive impairment.

To investigate the presence of peripersonal neglect, the conventional part of the Behavioural Inattention Test (BIT; Wilson, Cockburn, & Halligan, 1987) was administered. Participants were assigned to the two groups (neglect or controls) on the basis of their performance in the bisection subtest and in at least one of the other subtests of the BIT (see Table 1). In addition, all patients performed ecological tasks to assess the presence of neglect in personal or extrapersonal (i.e., beyond reaching) space. Nine patients showed left neglect (N+ group), whereas the remaining eight patients had no sign of left neglect (N– group). One neglect patient (LL) was later excluded from the N+ group (see Section 2). The remaining eight N+ patients did

Table 1
Demographical and neuropsychological data of the participants

	Group																
	N+	N+	N+	N+	N+	N+	N+	N+	N+	N–	N–	N–	N–	N–	N–	N–	N–
Patient	LT	CG	MS	GM	LBr	TGA	AM	PZg	LL	TS	VP	EB	PZr	DDC	DC	SM	AV
Age (years)	60	73	74	73	72	69	32	49	44	82	53	56	25	51	48	63	61
Education (years)	5	8	3	13	5	5	13	13	13	5	13	18	13	8	5	13	13
Sex	F	M	F	F	F	F	M	M	F	F	F	F	M	M	F	M	F
Lesion site ^a	F, P	F, I, T, P	F, P	F, I, T, BG	Th	F, P	F, P	F, P, T	F, I	F, P	BG	F	IC	BG	BG	PV	BG
Aethiology ^b	H	I	H	I	H	H	H	H	H	H	H	H	I	H	H	I	I
MMSE	24	21	21	26	20	21	23	28	24	22	30	30	30	27	23	29	29
Time from lesion ^c	763	65	56	22	1014	123	39	56	51	38	71	71	51	40	54	33	88
BIT (total)	49	32	40	141	107	114	103	43	67	138	145	140	146	145	133	144	141
BIT subtests																	
Line cancellation (18–18) c.o. 34	2–18	0–13	0–18	18–18	18–16	18–18	18–18	0–16	9–15	18–18	18–18	18–18	18–18	18–18	18–18	18–18	18–18
Letter cancellation (20–20) c.o. 32	0–13	0–5	2–8	20–20	13–10	19–19	5–17	0–5	5–9	18–17	20–20	19–20	20–20	20–20	16–17	20–18	18–17
Star cancellation (27–27) c.o. 51	0–9	0–14	0–6	27–26	21–18	8–24	10–24	0–13	5–18	27–26	26–27	25–24	27–27	26–27	23–26	27–27	27–27
Copying c.o. 3 ^d	3	0	1	3	3	2	3	2	0	4	4	4	4	4	4	4	4
Line bisection ^e c.o. 7	2-R	0-R	4-R	7-R	6-R	6-R	6-R	5-R	6-R	8-L	9	9	9	9	9	9	9
Drawing c.o. 2 ^d	2	0	1	2	2	0	2	2	0	2	3	3	3	3	2	3	3

BIT subtests: in parentheses the maximum score (number of items to be cancelled on the left and on the right, respectively). c.o.: cut off (pathological if \leq).

^a Th: thalamus; T: temporal; P: parietal; BG: basal ganglia; I: insula; F: frontal; O: occipital; IC: internal capsule; PV: paraventricular.

^b H: haemorrhagic; I: ischaemic.

^c In days.

^d Four copying and three drawing tasks. One point is given for each task if performance does not reveal important asymmetries.

^e R: bisection error rightwards; L: bisection error leftwards. Bisection of each of the three lines in the subtest is scored from 0 to 3 according to the accuracy of performance.

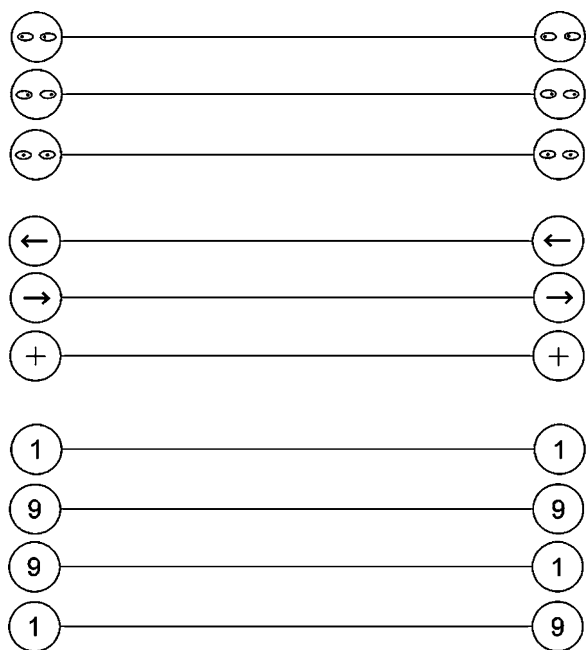


Fig. 1. Stimuli in the 10-cueing conditions. Each to-be-bisected line was printed in the centre of a separate A4 blank sheet.

not differ from the eight N- patients for age $F(1, 14) = 1.02$, n.s., education $F(1, 14) = 1.7$, n.s., and time since lesion, $F(1, 14) = 2.34$, n.s., whereas they differed for the BIT score, $F(1, 14) = 17.7$, $p < .001$.

1.2. Stimuli

Stimuli were black lines (200-mm-long and 0.5-mm-thick), printed on blank, horizontally oriented A4 sheets. A circle (diameter: 18 mm) was placed at the ends of each line to reduce perceptual asymmetries. Centred in each circle there was the cue, that belonged to one of the three categories: arrows, gazing eyes, or digits (see Fig. 1). Arrows pointed leftwards or rightwards. Eyes were gazing leftwards or rightwards. Two non-directional stimuli, a cross and eyes gazing straight ahead, were included as control for arrow and eye-gaze conditions, respectively. Digits were placed at the ends of the line according to two different schemes to test whether their magnitude would modulate the line bisection judgement independently of their spatial position. Thus, in one condition the same digit (1 or 9) was placed at both ends (hereafter, “digit magnitude” condition). In the other condition the digits 1 and 9 were placed at the two ends (hereafter, “digit number-line” condition) and their position was either congruent (i.e., 1-9) or incongruent (i.e., 9-1) with the left-to-right orientation of the mental number line.

1.3. Procedure

Each patient was presented with a set of 100 randomized single lines (i.e., 10 lines for each cueing condition). The midpoint of the to-be-bisected line was aligned with the midline of the patient’s trunk. Participants were asked to bisect each line by placing a mark with a pen. Cues were irrelevant for the task and

their presence was not mentioned in the instructions. Patients were free to move their head and eyes and they had no time limit to perform the task. The experiment took place in a single session (duration range: 15–35 min).

2. Results

For each bisected line we calculated the difference (in mm) between judged and true midpoints. Rightward shifts are represented by positive numbers, whereas leftward shifts are represented by negative numbers. Responses were approximated to the nearest mm. We then computed the median bisection error for each participant and condition (i.e., across the 10 trials in each condition). Fig. 2 shows the average bisection error for the two groups of patients (N+ vs. N-). We excluded the results of one neglect patient (LL) who showed a standard deviation (34.1 mm) that was four times higher than the mean of the other eight N+ patients (8.9 mm). Her responses ranged between 80 mm to the left and 62 mm to the right of the true midpoint, suggesting that she probably failed to follow the instructions.

An omnibus analysis of variance (ANOVA) was carried out with Cue Type (eyes vs. arrows vs. digit magnitude vs. digit number-line) and Cue Direction (leftwards vs. rightwards) as within-participants factors and Group (N+ vs. N-) as between-participants factor. The main effect of Group was significant, indicating a general rightward bisection bias for N+, $F(1, 14) = 5.73$, $p < .05$ (18 mm for N+ vs. 0.6 mm for N-). The two-way interaction Cue Type \times Cue Direction was marginally significant, $F(3, 42) = 2.76$, $p = .054$, suggesting that the cues were differentially effective. The interaction Cue Direction \times Group was also significant, $F(1, 14) = 6.99$, $p < .05$, indicating cueing effects in the N+ group only (N+: leftwards cueing = 17.2 mm vs. rightwards cueing 18.9 mm; N-: leftwards cueing = 0.8 mm vs. rightwards cueing = 0.5 mm). However, this was qualified by a significant three-way interaction Cue Type \times Cue Direction \times Group, $F(3, 42) = 2.98$, $p < .05$, indicating that the cueing effect in N+ varied as a function of the type

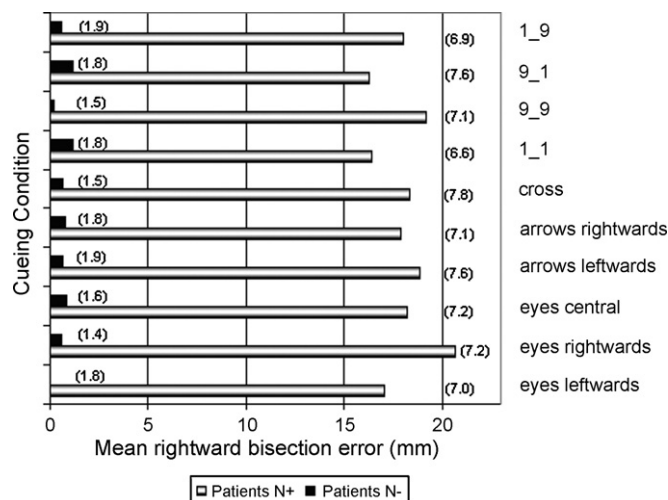


Fig. 2. Mean bisection error for the two groups of patients (N+ vs. N-). Positive values indicate a rightward shift. Standard error of the mean is shown in parentheses.

of cue (see Fig. 2). We therefore performed separate analyses for the four types of cue (eye gaze, arrows, digit magnitude, and digit number-line) and the two groups (N+ and N-).

For “eye gaze”, the ANOVA had three levels because it also included the straight-ahead gaze condition. The effect of gaze direction was close to significance in N+, $F(2, 14) = 3.64$, $p = .053$ but not in N-, $F(2, 14) = 1.03$, n.s. Mean bisection error for N+ was 17.1 mm for leftward gazing eyes, 20.7 mm for rightwards gazing eyes, and 18.3 mm for the straight-ahead gaze condition. For N-, mean error was 0 mm for leftward gazing eyes, 0.6 mm for rightward gazing eyes, and 0.8 mm for the straight-ahead gaze condition. The crucial contrast between leftward and rightward gaze was significant in N+, $t(7) = 5.01$, $p < .01$, one-tailed, but not in N-, $t(7) = 1.05$, n.s., one-tailed. None of the comparisons with the straight-ahead gaze reached significance (all p 's $> .05$).

For “arrows”, the ANOVA had three levels because it also included the (neutral) cross-condition. Cue Direction was not significant, neither in N+, $F(2, 14) = 0.27$, n.s. (18.9 mm for leftwards arrows, 17.9 mm for rightwards arrows and 18.4 mm for the cross-condition) nor in N-, $F(2, 14) = 0.05$, n.s. (0.6 mm for leftwards arrows, 0.8 mm for rightwards arrows, and 0.6 mm for the cross-condition). Also the direct comparison between leftward and rightward arrow conditions was not significant both in N+, $t(7) = -.76$, n.s., two-tailed and in N- $t(7) = 0.42$, n.s., two-tailed. All comparisons of the two arrow conditions with the non-directional cross-condition were non-significant. Note that the results of the N+ group, although far from being significant, are coherent with previous findings on healthy participants that showed a shift towards the direction opposite to that indicated by the arrow (e.g., Macdonald-Nethercott et al., 2000).

For the “digit magnitude” condition, the contrast between the two cues (i.e., 1-1 vs. 9-9) revealed a significant effect in N+, $t(7) = -1.97$, $p < .05$, one-tailed. Indeed, the rightward bias was smaller for the digit cue 1 (16.4 mm) compared to the digit cue 9 (19.2 mm). The same comparison performed on the data of the N- group was not significant, $t(7) = 2.12$, n.s., one-tailed. Note that the direction of the effect in N- was opposite to the expected one (1.2 mm for digit 1 and 0.2 mm for digit 9).

For the “digit number-line” condition, the contrast between the two cues (i.e., 1-9 vs. 9-1) did not reach significance, neither in N+, $t(7) = 1.26$, $p = .13$, one-tailed, nor in N-, $t(7) = -1.10$, $p = .32$, n.s., one-tailed. The results of the N+ group, however, showed a non-significant trend in a direction compatible with previous findings on healthy participants. That is, the rightward bias was larger when the digit cue 9 was on the right side of the visual line (16.3 mm for 9-1 vs. 18 mm for 1-9).

In summary, the rightward bias of neglect patients was selectively modulated by the direction of eye gaze and by the magnitude of two identical digits. The bisection error was shifted contralesionally by leftward-gazing eyes and “small” digits, whereas it was shifted ipsilesionally by rightward-gazing eyes and “large” digits. The effect of irrelevant eye gaze and digits on the performance of the individual neglect patients is shown in Fig. 3.

Neglect has been shown to affect the line bisection task mainly in terms of deviation from the true midpoint. However,

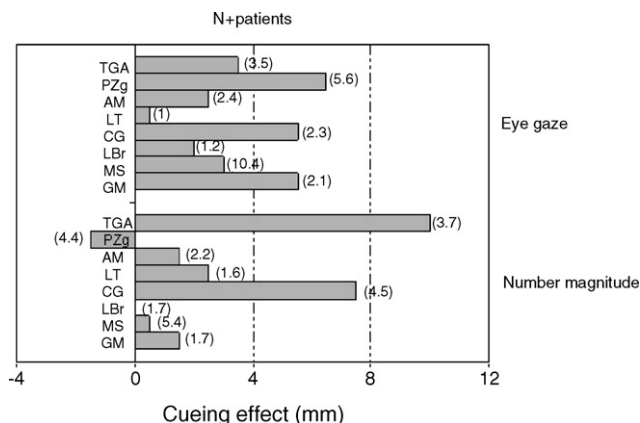


Fig. 3. Modulation of the bisection performance in individual N+ patients for eye gaze and digit magnitude conditions. Bars represent the cueing effect (i.e., rightward cue minus leftward cue bisection error). Standard error of the mean is shown in parentheses.

the performance of neglect patients can be analysed also in terms of variability (e.g., Marshall & Halligan, 1989). Thus, we investigated whether the severity of neglect can directly influence bisection performance both in terms of error and variability. To avoid any biases due to the selective effect of cueing in N+, we calculated the standard deviation for each condition separately and used these values to calculate the mean standard deviation for each patient. A one-way ANOVA on the mean standard deviation of the bisection error showed a higher variability in the N+ group (8.75 mm) in comparison to the N- group (3.45 mm), $F(1, 14) = 10.5$, $p < .01$, suggesting that the bisection performance is less consistent in neglect patients.

In addition, regression analyses (including both N+ and N- patients) revealed that the BIT score, indexing the presence and the severity of neglect, predicted the mean bisection error, $B = -0.30$, $R^2 = .60$, $F(1, 14) = 21.1$, $p < .001$, even when the performance in the bisection subtest was subtracted from the total BIT score, $B = -0.31$, $R^2 = .58$, $F(1, 14) = 19.6$, $p < .01$. Moreover, the BIT score predicted the mean standard deviation, $B = -0.078$, $R^2 = .67$, $F(1, 14) = 27.77$, $p < .001$. Thus, increased neglect severity was correlated not only with a more pronounced rightward shift but also with a less consistent performance in the line bisection task (see Fig. 4).

3. Discussion

Task-irrelevant cues had differential effects in modulating the line bisection performance of right brain damaged patients with left neglect. In contrast, all cues were ineffective with right brain damaged patients without neglect. Specifically, the overall rightward bias of neglect patients was modulated only by gaze cues and by the presence of two identical digits. The results will be now discussed separately for these two cue categories.

The effectiveness of gaze cueing has been related to its biological relevance. Eye gaze is a powerful cue because it can be an important source of social information (Argyle & Cook, 1976). Gaze direction may indicate the spatial position of an interesting event in the environment (i.e., food or danger) and may therefore

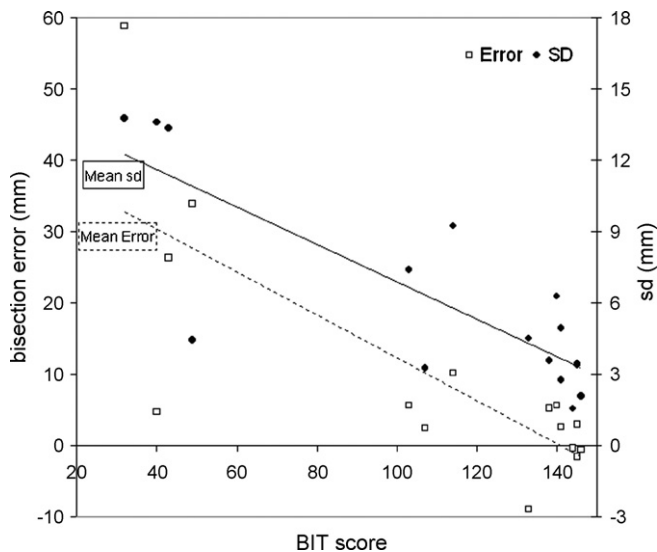


Fig. 4. Mean error and mean standard deviation in the bisection task for each patient as a function of the individual BIT score. Dotted and full lines represent the regression lines for error and standard deviation, respectively. Only 15 points are displayed because two patients had identical BIT scores (141) and average bisection error (2.6 mm).

activate a form of “joint attention” between two conspecifics (Butterworth & Jarrett, 1991). The cueing effects of eye gaze are pervasive, as shown by tasks where the cued location was responded to faster even though the cue was counterpredictive of the position of the target (Driver et al., 1999; Friesen, Ristic, & Kingstone, 2004). Accordingly, our finding that task-irrelevant gaze cues influence the bisection performance of neglect patients is consistent with the hypothesis that eye gaze has a “special status” with respect to the ability to reflexively orient spatial attention (e.g., Driver et al., 1999; Ricciardelli, Bricolo, Aglioti, & Chelazzi, 2002). However, it is worth noting that previous studies of healthy participants that directly compared eye gaze and arrow cues using detection or discrimination tasks have not provided a firm conclusion (Friesen et al., 2004; Gibson & Kingstone, 2006; Ristic, Friesen, & Kingstone, 2002). In contrast, the only previous study of right brain-damaged patients reported a consistent effect of gaze cues, but not of arrow cues, in modulating the extinction rate (Vuilleumier, 2002). The latter result is consistent with the findings of a recent fMRI study reporting that orienting to gaze cues and arrow cues is supported by partially distinct cortical networks (Hietanen, Nummenmaa, Nyman, Parkkola, & Hämäläinen, 2006). Moreover, orienting to gaze cues has been found in studies of infants as young as 3 months (Hood, Willen, & Driver, 1998).

It is important to note that in our experimental paradigm the gazing eyes were static and highly schematic. The study of Vuilleumier (2002) employed moving eyes that convey a motion cue (also see Friesen & Kingstone, 2003; Ricciardelli et al., 2002), which is a much stronger cue compared to static eyes (Farroni, Johnson, Brockbank, & Simion, 2000). Moreover, all previous studies investigated the effect of gaze cues on the detection of a lateralized stimulus in computer-based paradigms. Thus, our results show that the effect of gaze cues generalizes to a paper-and-pencil task carried out without time pressure.

The second type of cue that proved to be effective in our study was a pair of identical digits. It is important to stress that digits, as opposed to gaze cues, do not convey an explicit directional meaning. That is, the spatial coding of numbers takes place only at the semantic level, through the activation of a spatially oriented mental number line (Dehaene et al., 1993; Zorzi et al., 2002). Centrally presented digits have been shown to produce lateral shifts of spatial attention that are related to the numerical magnitude in studies of healthy participants (Casarotti et al., 2007; Fischer et al., 2003). However, the orienting effect appears to be reliable only when participants must attend to the digit cue (Casarotti et al., 2007). Moreover, it has been argued that digits possess a low degree of automaticity in orienting attention reflexively (Galfano, Rusconi, & Umiltà, 2006) and that the orienting effect reflects top-down control (Ristic, Wright, & Kingstone, 2006). However, our study shows that digits modulated the performance of neglect patients, even though they were completely irrelevant for the task. It is likely that the absence of time–pressure favoured the processing of the irrelevant digits and thus the access to the mental number line. This is consistent with previous studies of line bisection in healthy participants that demonstrated the effect of task-irrelevant digits (de Hevia et al., 2006; Fischer, 2001b).

It is however important to note that the effect of digit cues was reliable only when the same number was presented at both ends of the to-be-bisected line (i.e., the “digit magnitude” condition). The “number line” condition, in which the digits 1 and 9 were presented at the two ends, did not reliably modulate the rightward bias shown by neglect patients. The non-significant trend observed in the performance of neglect patients in the latter condition is compatible with the shift towards the larger number reported in previous studies with healthy participants (de Hevia et al., 2006; Fischer, 2001b). Notably, digits had a reliable effect only when both hemispaces were conveying the same numerical magnitude and, consequently, an identical spatial representation of number magnitude was activated. One possible explanation is that performance of the neglect patients was mostly influenced by the magnitude of the digit placed at the right end of the line, because the digit at the left end may have not been consciously processed. Nonetheless, implicit processing of the left digit would make performance less consistent.

Finally, the modulation observed in the digit magnitude condition confirms that implicit access to the mental number line is spared in neglect patients, as previously found by Priftis et al. (2006) using a SNARC task. That is, the disruption of the mental number line generated by neglect (Zorzi et al., 2002, 2006) is limited to tasks that require explicit access to and manipulation of the numerical magnitude (e.g., bisection of numerical intervals, Zorzi et al., 2002; or number comparison, Vuilleumier, Ortigue, & Brugger, 2004).

The effect of gaze cues and digits shows how a pathological phenomenon (i.e., the rightward bias) can be effectively modulated towards both contra- and ipsi-lesional directions. This finding resembles the results of Vallar, Daini and Antonucci (2000) and Daini et al. (2002), who asked neglect patients to bisect a line whose perceived length was manipulated by the presence of external in-ward or out-ward fins (resembling the

Brentano form of the Müller–Lyer illusion). Neglect patients' performance was modulated by the presence of the illusion. The finding that visual illusions (or, in our case, cueing) can be spared if not enhanced in the presence of neglect suggests an impairment of the attentional system monitoring the perceived line length (Daini et al., 2002). Indeed, cueing effects in our study were reliable in neglect patients but not in right brain damaged controls. The increased susceptibility to irrelevant cues shown by neglect patients might be interpreted as the result of an inconsistent perception of line length (as shown by the increased variability in bisection performance).

A final and more general point regards the overall bisection performance across patients. The severity of neglect, as indexed by the BIT score, predicted both the size of the rightward bias and the variability of performance (i.e., the standard deviation) across the entire patient sample. The correlation of neglect severity with bias size is not surprising, although the diagnostic value of line bisection was found to be much poorer with respect to cancellation tasks (Ferber & Karnath, 2001). The high correlation with variability of performance, instead, deserves a thorough discussion. Variability in line bisection, a feature that is far less studied than the classic rightward bias, has been taken as evidence for a pathologically extended "indifference zone" (Marshall & Halligan, 1989). The "indifference zone" theory suggests that the bisection bias is due to an increased Weber fraction, thereby increasing the discrepancy between two line lengths which are judged as equal in length. This hypothesis, first proposed to account for the effect of line length, was later found to fit with the inconsistent perception of the line centre in neglect (Olk, Wee, & Kingstone, 2004). Marshall and Halligan's (1989) single case study left open the question of whether the increased "indifference zone" could be attributed to neglect or to a general effect of brain damage. Olk et al. (2004) reported that an increased indifference zone in the Landmark task was related to the presence of neglect, but their small sample of patients with neglect ($N=3$) did not allow them to assess the existence of a significant correlation. Our larger sample allowed us to establish that neglect severity is directly related to the size of the indifference zone. In other words, the severity of neglect would determine the individual Weber fraction in line perception. It is worth noting that variability in line bisection was reliably measured because our paradigm implied the presentation of a high number of stimuli with a fixed line length. Increasing variability in line bisection appears therefore as a stable, although subtle, marker of neglect.

Acknowledgements

This study was supported by grants from MIUR (PRIN 2004 to M.Z.) and from the European Commission (Marie Curie Research Training Network "Numeracy and Brain Development" to M.Z.). We are grateful to Massimo Iannilli, Luca Ortolani, Carla Piubelli, Umberto Sansubrinio, Iaria Strumendo, and Marco Ferraro for referring patients under their care and for helpful comments.

References

- Argyle, M., & Cook, M. (1976). *Gaze and mutual gaze*. New York: Cambridge University Press.
- Bisiach, E., Capitani, E., Colombo, A., & Spinnler, H. (1976). Halving a horizontal segment: A study on hemisphere-damaged patients with cerebral focal lesions. *Archives Suisses de Neurologie, Neurochirurgie et de Psychiatrie*, *118*, 199–206.
- Butterworth, G., & Jarrett, N. (1991). What minds have in common is space: Spatial mechanisms serving joint visual attention in infancy. *British Journal of Developmental Psychology*, *9*, 55–72.
- Calabria, M., & Rossetti, Y. (2005). Interference between number processing and line bisection: A methodology. *Neuropsychologia*, *43*, 779–783.
- Casarotti, M., Michielin, M., Zorzi, M., & Umiltà, C. (2007). Temporal order judgement reveals how number magnitude affects visuospatial attention. *Cognition*, *102*, 101–117.
- Chieffi, S. (1999). Influence of perceptual factors on line bisection. *Cortex*, *35*, 523–536.
- Daini, R., Angelelli, P., Antonucci, G., Cappa, S., & Vallar, G. (2002). Exploring the syndrome of spatial unilateral neglect through an illusion of length. *Experimental Brain Research*, *144*, 224–237.
- Dehaene, S., Bossini, S., & Giraux, P. (1993). The mental representation of parity and number magnitude. *Journal of Experimental Psychology: General*, *122*, 371–396.
- de Hevia, M. D., Girelli, L., & Vallar, G. (2006). Numbers and space: A cognitive illusion? *Experimental Brain Research*, *168*, 254–264.
- Driver, J., Davis, G., Ricciardelli, P., Kidd, P., Maxwell, E., & Baron-Cohen, S. (1999). Gaze perception triggers reflexive visuospatial orienting. *Visual Cognition*, *6*, 509–540.
- Farroni, T., Johnson, M. H., Brockbank, M., & Simion, F. (2000). Infants' use of gaze direction to cue attention: The importance of perceived motion. *Visual Cognition*, *7*, 705–718.
- Ferber, S., & Karnath, H. O. (2001). How to assess spatial neglect—Line Bisection or cancellation tasks? *Journal of Clinical and Experimental Neuropsychology*, *23*, 599–607.
- Fias, W., & Fischer, M. H. (2005). Spatial representation of numbers. In J. A. D. Campbell (Ed.), *Handbook of mathematical cognition* (pp. 43–54). New York: Psychology Press.
- Fischer, M. H. (2001a). Cognition in the bisection task. *Trends in Cognitive Sciences*, *5*, 460–462.
- Fischer, M. H. (2001b). Number processing induces spatial performance biases. *Neurology*, *57*, 822–826.
- Fischer, M. H., Castel, A. D., Dodd, M., & Pratt, J. (2003). Perceiving numbers causes spatial shifts of attention. *Nature Neuroscience*, *6*, 555–556.
- Friesen, C. K., & Kingstone, A. (1998). The eyes have it! Reflexive orienting is triggered by non-predictive gaze. *Psychonomic Bulletin & Review*, *5*, 490–495.
- Friesen, C. K., & Kingstone, A. (2003). Abrupt onsets and gaze direction cues trigger independent reflexive attentional effects. *Cognition*, *87*, B1–B10.
- Friesen, C. K., Ristic, J., & Kingstone, A. (2004). Attentional effects of counter-predictive gaze and arrow cue. *Journal of Experimental Psychology: Human Perception and Performance*, *30*, 319–329.
- Galfano, G., Rusconi, E., & Umiltà, C. (2006). Number magnitude orients attention, but not against one's will. *Psychonomic Bulletin & Review*, *13*, 869–874.
- Gibson, B. S., & Kingstone, A. (2006). Visual attention and the semantics of space: Beyond central and peripheral cues. *Psychological Science*, *17*, 622–627.
- Halligan, P. W., Fink, G. R., Marshall, J. C., & Vallar, G. (2003). Spatial cognition: Evidence from visual neglect. *Trends in Cognitive Sciences*, *7*, 125–133.
- Heilman, K. M., & Valenstein, E. (1979). Mechanisms underlying hemispatial neglect. *Annals of Neurology*, *5*, 166–170.
- Hietanen, J. K., Nummenmaa, L., Nyman, M., Parkkola, R., & Hämäläinen, H. (2006). Automatic attention orienting by social and symbolic cues activate different neural networks: An fMRI study. *NeuroImage*, *33*, 406–413.

- Hood, B. M., Willen, J. D., & Driver, J. (1998). Adult's eye trigger shifts of visual attention in human infants. *Psychological Science*, *9*, 131–134.
- Hubbard, E. M., Piazza, M., Pinel, P., & Dehaene, S. (2005). Interactions between number and space in parietal cortex. *Nature Reviews Neuroscience*, *6*, 435–448.
- Ishihara, M., Jacquin-Courtois, S., Flory, V., Salemme, R., Imanaka, K., & Rossetti, Y. (2006). Interaction between space and number representation during motor preparation in manual aiming. *Neuropsychologia*, *44*, 1009–1016.
- Jewell, G., & McCourt, M. E. (2000). Pseudoneglect: A review and meta-analysis of performance factors in line-bisection tasks. *Neuropsychologia*, *38*, 93–110.
- Kashmere, J. L., & Kirk, A. (1997). The complex interaction of normal biases in line bisection. *Neurology*, *49*, 887–889.
- Macdonald-Nethercott, E. M., Kinnear, P. R., & Venneri, A. (2000). Effect of a directional cue on line bisection. *Brain and Cognition*, *43*, 325–328.
- Magni, E., Binetti, G., Padovani, A., Cappa, S. F., Bianchetti, A., & Trabucchi, M. (1996). The Mini-Mental State Examination in Alzheimer's disease and multi-infarct dementia. *International Psychogeriatrics*, *8*, 127–134.
- Marshall, J. C., & Halligan, P. W. (1989). When right goes left: An investigation of line bisection in a case of visual neglect. *Cortex*, *25*, 503–515.
- Nichelli, P., Rinaldi, M., & Cubelli, R. (1989). Selective spatial attention and length representation in normal subjects and in patients with unilateral spatial neglect. *Brain and Cognition*, *9*, 57–70.
- Olk, B., & Harvey, M. (2002). Effects of visible and invisible cueing on line bisection and Landmark performance in hemispacial neglect. *Neuropsychologia*, *40*, 282–290.
- Olk, B., Wee, J., & Kingstone, A. (2004). The effect of hemispacial neglect on the perception of centre. *Brain and Cognition*, *55*, 365–367.
- Parton, A., Malhotra, P., & Husain, M. (2004). Hemispacial neglect. *Journal of Neurology, Neurosurgery, and Psychiatry*, *75*, 13–21.
- Priftis, K., Zorzi, M., Meneghello, F., Marenzi, R., & Umiltà, C. (2006). Explicit versus implicit processing of representational space in neglect: Dissociations in accessing the mental number line. *Journal of Cognitive Neuroscience*, *18*, 680–688.
- Ricciardelli, P., Bricolo, E., Aglioti, S. M., & Chelazzi, L. (2002). My eyes want to look where your eyes are looking: Exploring the tendency to imitate another individual's gaze. *NeuroReport*, *13*, 2259–2263.
- Riddoch, J. M., & Humphreys, G. W. (1983). The effects of cueing on unilateral neglect. *Neuropsychologia*, *21*, 589–599.
- Ristic, J., Friesen, C. K., & Kingstone, A. (2002). Are eyes special? It depends on how you look at it. *Psychonomic Bulletin and Review*, *9*, 507–513.
- Ristic, J., & Kingstone, A. (2006). Attention to arrows: Pointing to a new direction. *Quarterly Journal of Experimental Psychology*, *59*, 1921–1930.
- Ristic, J., Wright, A., & Kingstone, A. (2006). The number line effect reflects top-down control. *Psychonomic Bulletin and Review*, *13*, 862–868.
- Schenkenberg, T., Bradford, D. C., & Ajax, E. T. (1980). Line bisection and unilateral visual neglect in patients with neurological impairments. *Neurology*, *30*, 509–517.
- Vallar, G. (2001). Extrapersonal visual unilateral spatial neglect and its neuroanatomy. *Neuroimage*, *14*, 52–58.
- Vallar, G., Daini, R., & Antonucci, G. (2000). Processing of illusion of length in spatial hemineglect. A study of the line bisection. *Neuropsychologia*, *38*, 1087–1097.
- Vuilleumier, P. (2002). Perceived gaze direction in faces and spatial attention: A study in patients with parietal damage and unilateral neglect. *Neuropsychologia*, *40*, 1013–1026.
- Vuilleumier, P., Ortigue, S., & Brugger, P. (2004). The number space and neglect. *Cortex*, *40*, 399–410.
- Wilson, B., Cockburn, J., & Halligan, P. W. (1987). *The behavioural inattention test*. Bury St. Edmunds, UK: Thames Valley Test Company.
- Zorzi, M., Mapelli, D., Rusconi, E., & Umiltà, C. (2003). Automatic spatial coding of perceived gaze direction is revealed by the Simon effect. *Psychonomic Bulletin & Review*, *2*, 423–429.
- Zorzi, M., Priftis, K., Meneghello, F., Marenzi, R., & Umiltà, C. (2006). The spatial representation of numerical and non-numerical sequences: Evidence from neglect. *Neuropsychologia*, *44*, 1061–1067.
- Zorzi, M., Priftis, K., & Umiltà, C. (2002). Brain damage: Neglect disrupts the mental number line. *Nature*, *417*, 138–139.