Functional independence between numerical and visual space: evidence from right-brain damaged patients

Published version:

DOI:10.1016/j.cortex.2012.04.005

Functional independence between numerical and visual space: Evidence from right brain-damaged patients

Lorenzo Pia[1], Marco Neppi-Mòdona, Luigi Cremasco, Patrizia Gindri, Olga Dal Monte, Alessia Folegatti

[1]Psychology Department, University of Turin, Italy. lorenzo.pia@unito.it

Abstract

What is the relationship between numerical and visual space? Here we tried to shed new light on this debated issue investigating whether and how the two forms of representation are associated or dissociated when co-activated. We carried out a series of visual-numerical bisection experiments on a large group of right brain-damaged patients ($N = 32$) with and without left neglect. We examined (a) the degree of association between the pathological rightward error in the bisection of numerical intervals and left neglect (Experiment 1); (b) if the size of the numerical interval modulates spatial errors in bisection tasks in which numerical and visual space representations are co-activated (Experiment 2). The results showed that (a) numerical bisection error and left spatial neglect are doubly dissociated and that, when both are present, they are not correlated; (b) the size of the numerical interval did not affect the spatial bisection error but influenced the numerical bisection error. These data suggest that attentional processes involved in the navigation along visual space and numerical internal representations are independent neurocognitive operations. We must emphasize that our findings should be taken with caution because they are based mainly on negative results.

1. Introduction

It has been suggested that the representation of numerical quantities can be likened to a continuous, non-verbal, mental number line with smaller quantities located to the left of larger ones. Hence, the same attentive mechanisms that operate to select locations in space would be engaged when attending to quantities along the mental number line (Dehaene et al., 2003; Hubbard et al., 2005; Umilta et al., 2009).

Evidence in favor of this hypothesis was first reported by Zorzi and coworkers (Zorzi et al., 2002) in patients with left spatial neglect, i.e., a deficit of attention and awareness of the left space, which usually follows lesions to the right inferior parietal lobe and parieto-frontal connections in the underlying white matter (see Bartolomeo et al., 2007 for a review). Zorzi and coworkers found that when neglect patients are asked to verbally report the numerical midpoint between two orally presented numbers, they misplace the subjective midpoint progressively rightwards as the interval grows (e.g., numerical midpoint of interval 1−9 = 8 instead of 5), along with a paradoxical leftward displacement ("crossover effect") for smaller intervals (e.g., numerical midpoint of interval 1−3 = 1 instead of 2). Since the pattern of numerical error mimicked the one usually reported in the bisection of horizontal visual lines [i.e., progressive rightwards misplacement of the midpoint as line length increases and crossover with short line lengths (e.g., Chatterjee, 1995)], Zorzi and coworkers (Zorzi et al., 2006, 2002) interpreted their findings in terms of a deficit of spatial representation for numerical quantities located to the left of a reference point along the mental number line. This, in turn, would support the view that the neurocognitive mechanisms involved in shifting spatial attention in external space and along the mental number line are the same.

A number of works have confirmed the presence of an ipsilesional numerical bisection bias both in right (Cappelletti et al., 2007; Doricchi et al., 2009, 2005; Priftis et al., 2006; Rossetti et al., 2004; Zamarian et al., 2007; Zorzi et al., 2006) and left (Pia et al., 2009) brain-damaged patients: however, many of these studies have found that the numerical bisection bias is dissociated from an equivalent visual spatial bias (Doricchi et al., 2009; Loetscher et al., 2009; Rossetti et al., 2004; van Dijck et al., 2011) both on a functional (Doricchi et al., 2009; Loetscher and Brugger, 2009; Rossetti et al., 2004; van Dijck et al., 2011) and on an anatomical (Doricchi et al., 2009, 2005) ground.

To provide an explanation for these dissociations, it was proposed (Umilta et al., 2009; Zorzi et al., 2006) that double dissociations between numerical and spatial errors do not necessarily imply that visual and numerical spaces are two distinct cognitive domains. Indeed, this claim is consistent with the fact that in neglect visual and representational space can be double dissociated [see (Bisiach and Vallar, 2000) for a review]. The abovementioned authors (Umilta et al., 2009; Zorzi et al., 2006) argued that the mental number line might be functionally isomorphic to visual lines. In other words, numerical line would have properties analogous to visual lines, namely they would be based on the same spatial metric. Nonetheless, the mental number line would still remain a form of representation in the imagined space, whereas visual lines a representation in the perceptual space. This hypothesis leads to very clear and easily testable predictions: if numerical and visual representations are isomorphic, they should influence each other when concurrently activated, namely number processing should affect spatial orienting and, viceversa, spatial processing should affect the numerical processing [see (Umilta et al., 2009; Zorzi et al., 2002) for more details].

In the present study, we firstly examined the relationship between presence/absence of a rightward error in the mental number line bisection task and presence/absence of left neglect on visual line bisection and target cancellation tasks (Experiment 1). Secondly, in those patients in whom a progressive rightward bisection error was present in the mental number line bisection task (distance effect), we analyzed whether numerical interval size affected spatial bisection biases in a paper and pencil bisection task in which numerical and visual space are co-activated (Experiment 2).

2. Experiment 1 – mental number line bisection task

2.1. Participants

Thirty two right-handed patients (10 women; mean age: 67.82 years, SD = 8.72 years; mean educational level: 8.44 years, SD = 3.25 years) with right hemisphere damage (confirmed by CT or MRI scans) participated in the study after having given written informed consent according to the Declaration of Helsinki. Demographic and clinical data are reported in Table 1.

Table 1 – Demographic and clinical data of right brain-damaged patients.

Subject	Sex	Age	Education (y)	Duration (days)	Etiology	Lesion (CT scan)	Neurological examination			MMSE	Mental number bisection	Line bisection	Diller	Groups	
							M	S	V					Mental number bisection	Neglect assessment
1	F	45	12	106	H	O, P, F, wm	3–2	3–3	3–3	26	.5	27.67	33	D+	N+
2	M	76	8	134	H	T, P, F, bg, wm	3–3	3–3	3–3	27	.22	19.67	6	D+	N+
3	F	80	5	152	I	T, P, bg	1–1	0–3	0–3	25	.11	27	14	D–	N+
4	M	67	5	960	I	P	3–3	3–2	3–2	27	.67	10.33	25	D+	N+
5	M	66	10	45	I	T, F, bg	0–0	0–0	0–0	25	.28	.67	0	D+	N–
6	M	62	8	57	I	O, T, P, I, F, bg	3–2	3–3	3–3	25	.89	–3	0	D+	N–
7	F	75	5	45	I	T, I, F, wm	3–3	1–1	1–1	24	1.11	7.67	10	D+	N+
8	M	62	13	109	I	T, P, I, F, wm	2–2	1–1	1–1	28	.67	–2	0	D+	N–
9	F	57	8	1450	M	T, Th, wm	0–0	0–0	0–0	25	.06	10.33	13	D–	N+
10	M	66	10	85	I	P, F, bg, wm	0–0	0–0	0–0	29	.83	11.33	10	D+	N+
11	F	68	8	186	H	Bg	3–1	3–0	3–0	24	.28	4.67	6	D+	N+
12	M	75	8	78	H	T, P, F, I, bg, wm	3–3	3–3	3–3	28	.17	70.67	25	D–	N+
13	M	67	13	91	I	Bg	3–3	3–3	3–3	25	0	71.67	5	D–	N+
14	F	73	8	25	I	T, P, Wm	2–2	1–2	1–2	24	.78	20.33	27	D+	N+
15	M	61	13	30	I	T, O, P	2–2	3–3	3–3	25	.78	31.33	27	D+	N+
16	M	66	8	89	I	F	2–2	1–1	1–1	24	.39	0	0	D+	N–
17	M	73	8	112	I	F	1–1	0–0	0–0	25	1.61	2	0	D+	N–
18	F	77	4	25	I	O, P	2–2	3–3	3–3	24	–.33	4.67	5	D–	N+
19	M	65	8	86	H	F, P, wm	2–1	0–0	0–0	28	.72	–3.67	0	D+	N–
20	F	72	5	50	I	F, bg	3–1	0–0	0–0	27	.06	–1.67	0	D–	N–
21	F	65	13	38	I	T	1–1	0–0	0–0	27	.06	1	0	D–	N–
22	M	68	8	147	I	T, wm	3–1	0–0	0–0	27	0	–3	0	D–	N–
23	F	60	8	67	I	th, bg, wm	0–0	0–0	0–0	28	.50	.33	0	D+	N–
24	M	75	5	49	H	th, hi	3–2	0–0	0–0	26	0	6.67	25	D–	N+
25	M	71	13	16	I	F, Wm	3–3	1–1	1–1	29	.22	–1.67	0	D+	N–
26	M	80	3	57	I	T, wm	1–1	0–0	0–0	29	0	1.67	0	D–	N–
27	M	47	13	138	I	Th	3–3	0–0	0–0	27	–.33	4.33	2	D–	N–
28	M	83	13	57	I	T, P, F, I, hi, wm	2–1	0–0	0–0	27	.5	1.33	0	D+	N–
29	M	76	5	117	H	Bg	1–1	0–0	0–0	24	0	4.67	5	D–	N+
30	M	59	13	27	H	Wm	3–1	0–0	0–0	30	–.11	6.67	5	D–	N+
31	M	69	10	28	I	th, wm, bg	1–3	0–0	0–0	28	.11	–2.67	–3	D–	N–
32	M	71	3	29	H	F, I	1–1	0–0	0–0	26	1.89	–4.67	0	D+	N–

Sex: M = Male, F = Female. Schooling: years (y) of formal education. Etiology: H = hemorrhage, I = ischemia, M = meningioma. Lesion: F = frontal, O = occipital, T = temporal, P = parietal, I = Insula, bg = basal ganglia, Th = thalamus, hi = hippocampus, wm = white matter. Neurological examination: Contralesional Motor (M), Somatosensory (S), and Visual half-field (V) neurological deficits (the two values refer to the upper and lower limb/visual quadrants respectively); scores ranged from normal (0) to severe defects (3). MMSE: Mini-Mental State Exam score (cut-off point < 24). Mental number bisection: mean difference (units) between the subjective and objective numerical midpoint; rightward and leftward errors were given positive and negative values respectively; the cut-off point was $\geq .203$ units, that is C group mean error (–.033 units) plus 2 SD. Line bisection: mean difference (mm) between the subjective and the objective midpoint; rightward and leftward errors were given positive and negative values respectively; the cut-off point was ≥ 3.954 mm, that is C group mean error (–.527) plus 2 SD. Diller: left minus right side omissions; the cut-off point was ≥ 4. Groups: patients were classified as deviating (D+) or non-deviating (D–) if their mean rightward error in the mental number bisection task was above the cut off; patients were classified as neglect (N+) or non-neglect (N–) if both their mean rightward error in the line bisection task and the score in the Diller were above the cut off.

A control group (C) of 30 healthy subjects (9 women; mean age: 62 years, SD = 6.61 years; mean educational level: 12 years SD = 4.35 years) matched with respect to age, sex and educational level [age: $t(62) = -.64$, $p = .524$; educational level: $t(62) = -.724$, $p = .472$, respectively] was also tested to establish cut-off scores (see legend of Table 1).

2.2. Stimuli and procedure

Participants were administered a mental number line bisection task and two traditional tests to assess the presence of left neglect: a visual line bisection and a letter cancellation task (Diller and Weinberg, 1977).

In the mental number line bisection task, participants were presented with two spoken number words that defined a numerical interval. The size of the interval could be three (e.g., 1–3), five (1–5), or nine (1–9) units. The magnitude of the two numbers could be units (e.g., 1–5), teens (11–15) or first teens (21–25). The order of presentation could be ascending (e.g., 1–5) or descending (5–1). The total number of stimuli was eighteen, randomly administered. We selectively administered intervals positioned at the beginning of decades [using a smaller number of trials respect to previous studies (Pia et al., 2009; Zorzi et al., 2002; Doricchi et al., 2005)] because these intervals show the highest sensitivity to numerical bisection biases induced by right brain damage (Doricchi et al., 2009). Participants were asked to state the numerical midpoint of any given interval without any calculation.

In the visual line bisection task, participants had to bisect five 180 mm long horizontal lines individually printed in the middle of an A4 landscape-oriented sheet of paper; in the letter cancellation task, they had to cancel 103 Hs among 208 distractor letters printed on an A3 landscape-oriented sheet of paper (see Table 1).

2.3. Results

The cut-off score of the mental number line bisection task was set at the level of the average deviation observed in the C group (i.e., numerical difference between the subjective and the objective midpoint) plus 2 SD (see Table 1). Eighteen patients (56.25%) were classified as deviating (D+; mean ≥ cut-off) and fourteen (43.75%) as non-deviating (D−; mean < cut-off). Then, in order to assess whether numerical errors increased as a function of interval size, we performed a repeated measures ANOVA on the numerical bisection error, with ‘interval size’ (three, five and nine) as within subjects factor and ‘group’ (D+ and D−) as between subjects factor. The two main factors as well as their interaction resulted significant: 'group' [$F(1, 30) = 33.02$, $p < .0001$]; 'interval size' [$F(2, 60) = 12.45$, $p < .0001$]; 'interval size' × 'group' [$F(2, 60) = 17.97$, $p < .0001$]. In the D+ group the numerical bisection error was displaced significantly more rightwards (mean = .71 units, SE = .08 units) than the D− group (mean = −.01 units, SE = .09 units). As for the factor 'interval size', a Newman–Keuls post-hoc analysis showed that the numerical error increased ($p < .05$ for all comparisons) as a function of interval size (interval three: mean = .08 units, SE = .08 units; interval five: mean = .29 units, SE = .07 units; interval nine: mean = .67 units, SE = .12 units). A Newman–Keuls post-hoc analysis on the 'group × size interaction' showed that only the D+ group displayed a significant ($p < .05$) rightward deviation of the midpoint number as a function of interval size: D+ interval three: mean = .16 units (SE = .109 units); D+ interval five: mean = .54 units (SE = .1 units), D+ interval nine: mean = 1.44 units (SE = .16 units); D− group interval three: mean = .005 units (SE = .12 units); D− group interval five: mean = .04 units (SE = .11 units); D− group interval nine: mean = −.09 units (SE = .17 units). In Fig. 1 is represented the mean numerical error (units) as a function of the interval size in D+ and D− patients.

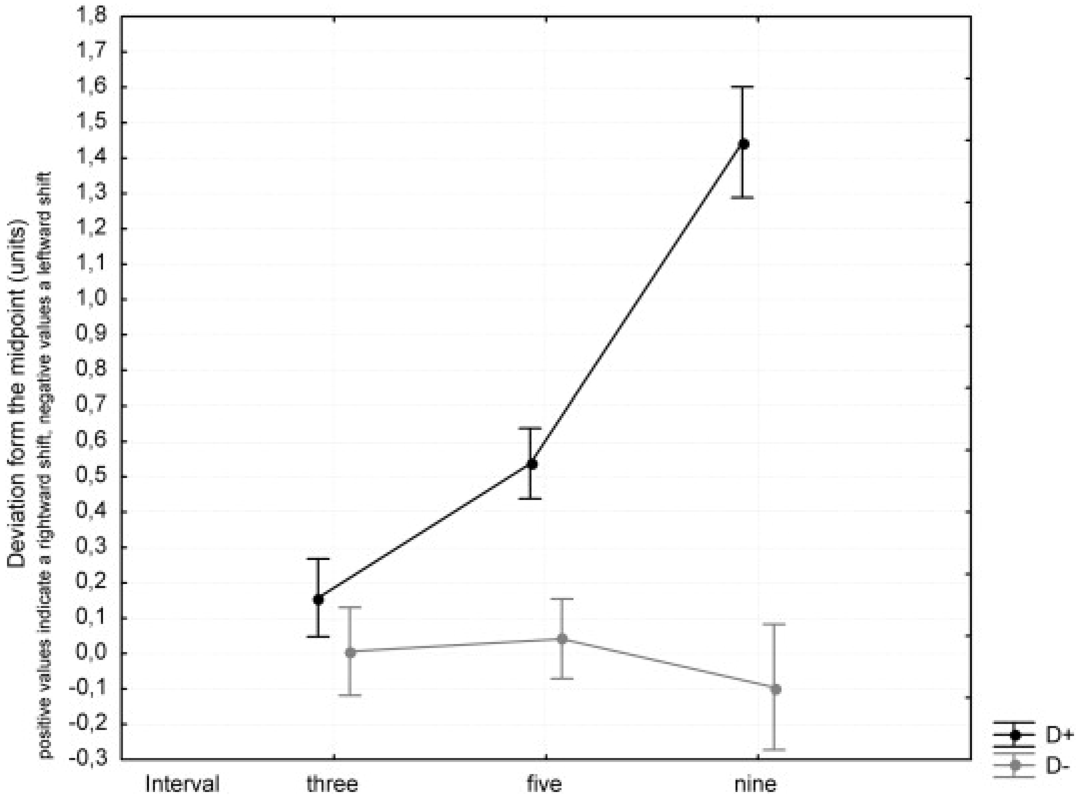

Fig. 1. Mental number line bisection task in D+ and D− patients. Mean numerical error (units) as a function of the interval size.

As regards with neglect assessment, the mean visual line bisection error of control subjects (spatial difference between the subjective and the objective midpoint) plus 2 SD, and a left–right difference in the number of omitted Hs ≥ 4 (Pizzamiglio et al., 1989) were set as cut-off scores (see legend of Table 1). According to these values, sixteen patients (50%) had neglect (N+; means ≥ cut-off) and sixteen (50%) had no neglect (N−; means < cut-off). A repeated measures ANOVA on the numerical bisection error, with 'interval size' (three, five and nine) as within subjects factor and 'group' (N+ and N−) as between subjects factor was performed. 'Interval size' resulted significant [$F\,(2, 60) = 10.69$, $p < .001$], whereas 'group' and 'interval size' × 'group' interaction were not. As for the factor 'interval size', a Newman–Keuls post-hoc analysis showed that the numerical error was highest ($p < .05$) with interval nine (mean = .78 units, SE = .17 units) respect to both interval five (mean = .32 units, SE = .08 units) and three (mean = .09 units, SE = .08 units). In Fig. 2 is represented the mean numerical error (units) as a function of the interval size in N+ and N− patients.

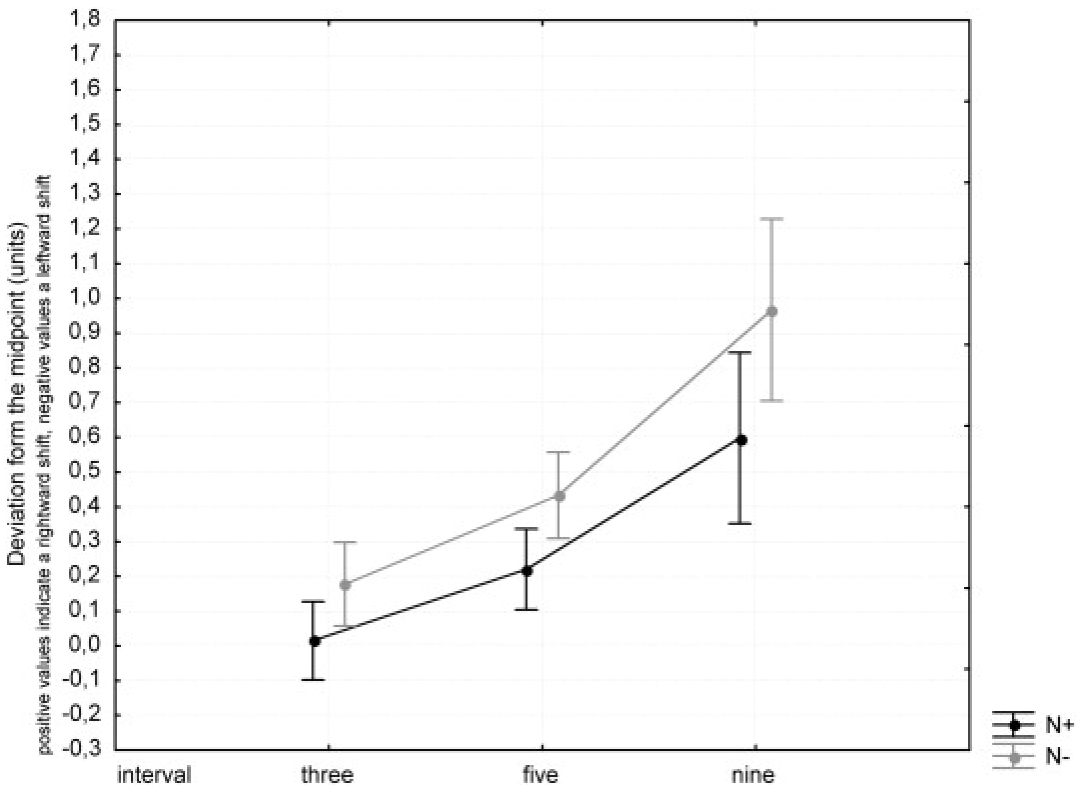

Fig. 2. Mental number line bisection task in N+ and N− patients. Mean numerical error (units) as a function of the interval size.

In order to assess whether presence of neglect and of the mental number line effect were associated, first (1) we compared the percentage of patients with (or without) a rightward numerical error with the percentage of patients with (or without) neglect (two tailed *t* tests on percentages); then (2), we computed the correlation among the number line bisection error and the two indexes of neglect severity (the visual line bisection error and the number of omitted Hs on the cancellation task) over the entire group of patients. (1) Eight patients (out of 32) were D+N+ (50%), eight were D−N+ (50%), ten D+N− (62.5%) and six D−N− (37.5%). The four crucial comparisons (i.e., D+N+ *vs* D+N−, D+N+ *vs* D−N+, D+N− *vs* D−N−, D−N+ *vs* D−N−) were not significant ($p > .05$); (2) the number line bisection error was not correlated to any of the two indexes of neglect severity (visual bisection: $n = 32$, Pearson's $r = .-148$, $p =$ n.s.; Omissions: $n = 32$; Pearson's $r = .038$, $p =$ n.s.). Interestingly, visual bisection error and the number of omissions were positively correlated ($n = 32$, Pearson's $r = .559$, $p = .001$).

2.4. Discussion

The results of Experiment 1 showed that although in right brain-damaged patients the rightward numerical error in the mental number line bisection task and visual neglect can co-occur, they seem to be independent: they have the same probability of occurring or not occurring together and, when they coexist, their severity is not correlated. It is worth noticing, the deviation we have observed in D+ patients on the bisection of 9-unit intervals, i.e., 1.44 units, is higher than that observed in previous studies administrating all the intervals included in each decade (e.g., Zorzi and coworkers, 2006 = .5 units; Doricchi and colleagues, 2005 = .7 units; Priftis and colleagues, 2006 = 1 unit; Doricchi and coworkers, 2009 = 1 unit). This confirms the higher sensitivity of the bisection task used in the present study, which selectively included intervals positioned at the beginning of decades.

3. Experiment 2 – visual–mental number line bisection task

In order to test the "functional isomorphism" hypothesis (Umilta et al., 2009; Zorzi et al., 2002), we run a second experiment only on D+N+ and D+N− patients in which we tested whether the size of the numerical interval influenced the spatial bisection error. This experiment was designed in order to induce a co-activation of visual and numerical space. Patients were given the same stimuli and conditions as in Experiment 1, but with the two numbers defining the numerical intervals printed on paper (for a similar task see Bonato et al., 2008).

3.1. Participants

Eighteen D+ patients according to the results of Experiment 1 (see Table 1).

3.2. Stimuli and procedure

Patients were administered a visual–mental number line bisection task with two response conditions and a baseline endpoints bisection task. This latter task was administered in order to test whether the classification in D+N+ and D+N− patients obtained by means of two traditional tests to assess neglect is maintained when patients are asked to bisect empty spaces.

In the endpoints bisection task, five couples of horizontally aligned black dots spaced out 180 mm and printed on an A4 landscape-oriented sheet of paper were presented to the patients. They were asked to indicate the midpoint of the empty space enclosed between the two dots.

In the visual–mental number line bisection task, two numbers defining a numerical interval (the same interval as in Experiment 1) were horizontally spaced out 180 mm on an A4 landscape-oriented sheet of paper. The physical distance between the two numbers delimiting the empty space enclosed between them was kept constant. In one condition, patients were simply asked to mark with a pencil the midpoint of the empty space enclosed between the two numbers. We called this condition 'implicit' because the mental number line would be (eventually) activated implicitly by task demands. Additionally, we administered a second condition, called 'explicit', in which patients were asked to mark the midpoint of the empty space enclosed between the two numbers by *writing down the number that is numerically halfway between the two numerical extremes*. The rationale to add this second condition was that some data suggest that the spatial coding of numbers takes place only at a semantic level, through an explicit activation of a spatially oriented mental number line (Dehaene et al., 1993, 2003). As in Experiment 1, the total number of stimuli in each of these two conditions was eighteen randomly administered. The two conditions were counterbalanced across subjects and administered in the same testing session of Experiment 1.

Two predictions can be made: (1) if number processing affects spatial orienting, as suggested by the functional isomorphism hypothesis, both spatial and numerical errors should be biased progressively more rightward as a function of the numerical interval size increment; (2) if there is no isomorphism between numerical and visual spatial representations, instead, only numerical errors should be modulated by numerical interval size.

3.3. Results

As regards as the endpoint task, the mean bisection error (spatial difference between the subjective and the objective midpoint) was significantly different between D+N+ and D+N− on an independent sample *t* test: $t\,(16) = 2.557$, $p < .05$. The D+N+ group bisected more rightward (mean 10 mm; SD = 7.9) than the D+N− group (mean = −.9 mm; SD = 9.8).

We performed a first repeated measures ANOVA on the spatial bisection error (spatial difference between the subjective and the objective midpoint) as dependant variable with ‘interval size’ (three, five and nine) and ‘task demands’ (implicit, explicit) as within subjects factors, and ‘group’ (D+N+ and D+N−) as between subjects factor. Only the main factor ‘group’ resulted significant [$F\,(1,\ 16) = 9.26$, $p < .05$], with the D+N+ group bisecting significantly more rightward (mean = 7.8; SE = 3.1) respect to the D+N− group (mean = −.5; SE = −2.8). All the other factors as well as their interactions were not significant ($p > .05$). In Fig. 3 is represented the mean spatial error (mm) as a function of the interval size and task demand in D+N+ and D+N− patients.

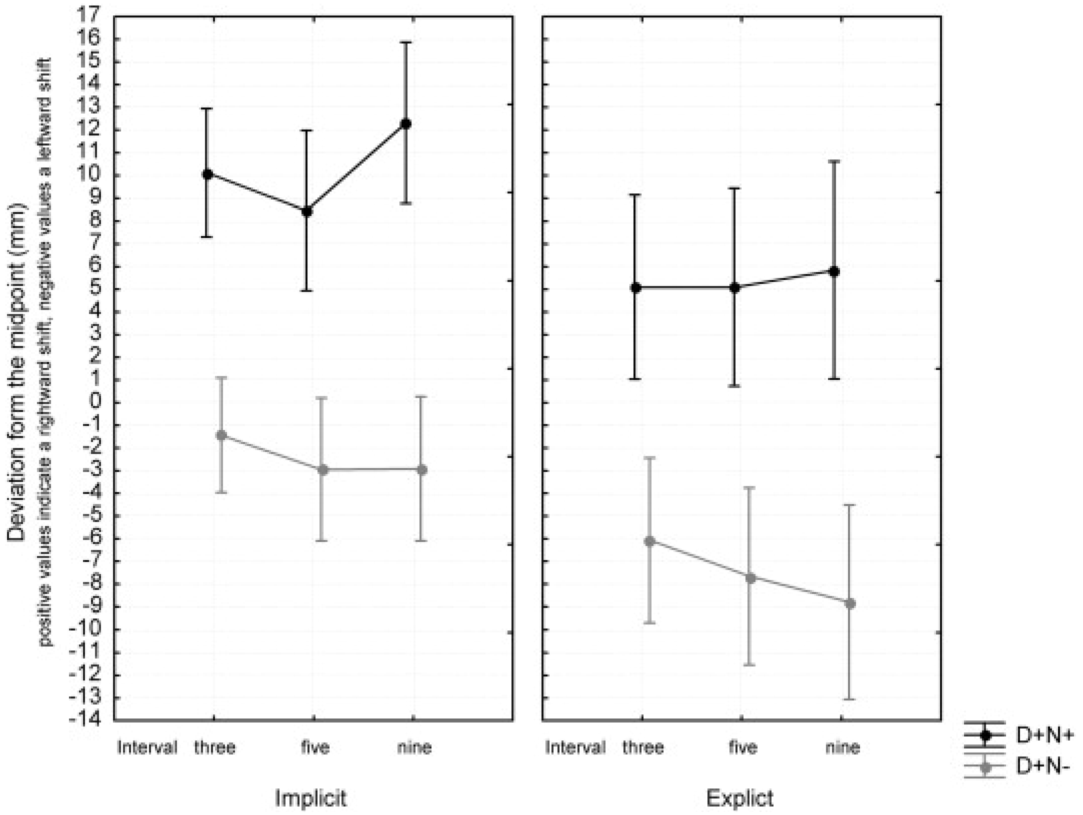

Fig. 3. Visual–mental number line bisection task in D+N+ and D+N− patients. Mean spatial error (mm) as a function of the interval size and task demand.

We performed a second repeated measure ANOVA on the numerical bisection error (numerical difference between the subjective and the objective midpoint) as dependent variable with ‘interval size’ (three, five and nine) as within subjects factor and ‘group’ (D+N+ and D+N−) as between subjects factor. Only the factor ‘interval size’ resulted significant [$F\,(2,\ 32) = 5.241, p < .05$]. A Newman–Keuls post-hoc analysis ($p < .05$) showed that the numerical error increased as a function of interval size (interval three: mean = .121, SE = .064; interval five: mean = .473, SE = .167; interval nine: mean = .833, SE = .198). Moreover, in order to test whether the visual–mental number line bisection task is comparable to traditional mental number line bisection task (i.e., Experiment 1), we performed a third repeated measures ANOVA on the numerical bisection error adding ‘experiment’ (Experiment 1, Experiment 2) as within subjects factor. Again, only the factor ‘interval size’ resulted significant [$F\,(2, 32) = 25.684, p < .05$]. A Newman–Keuls post-hoc analysis ($p < .05$) showed that the numerical error increased as a function of interval size (interval three: mean = .13, SE = .009; interval five: mean = .05, SE = .09; interval nine: mean = 1.14, SE = .15). All the other factors as well as interactions were not significant with $p > .05$. In Fig. 4 is represented the mean numerical error (units) as a function of the interval size and task demand in D+N+ and D+N− patients.

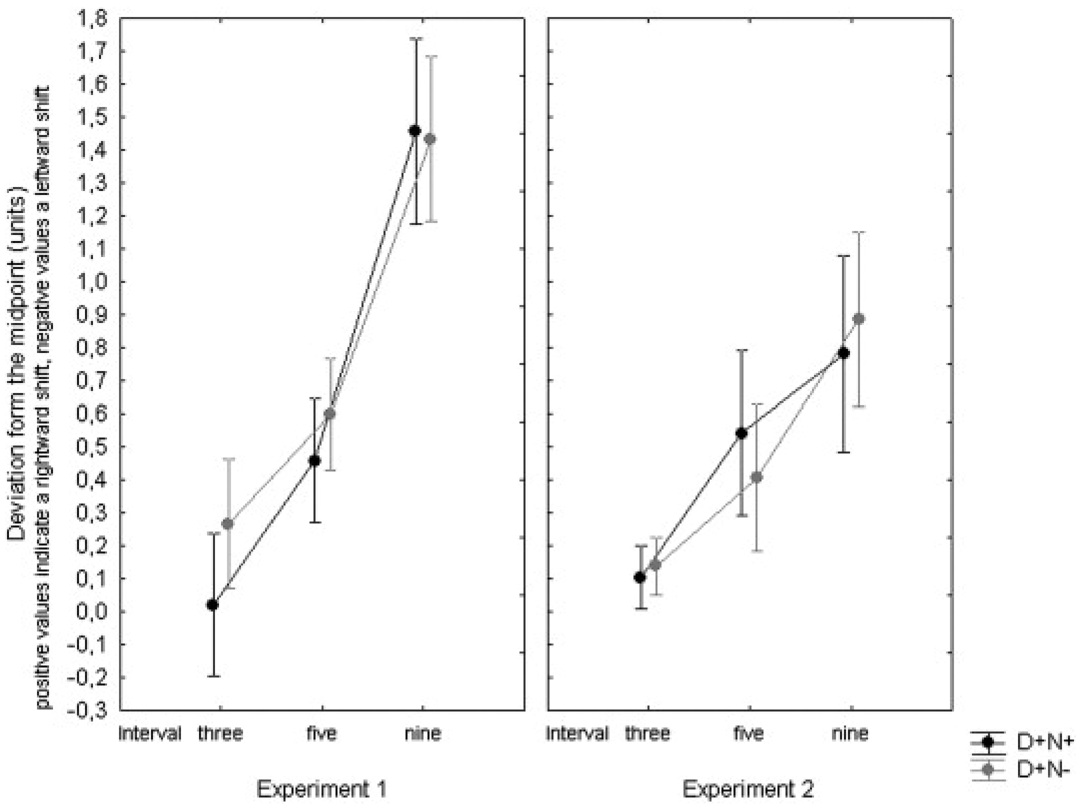

Fig. 4. Visual–mental number line bisection task and mental number line bisection task in D+N+ and D+N− patients. Mean numerical error (units) as a function of the interval size.

3.4. Discussion

The results of Experiment 2 showed that when numerical and visual space representations are co-activated, the size of the numerical interval selectively modulates the numerical bisection bias of D+ patients with no effect on the spatial bisection bias. Importantly, this result was independent of the presence or absence of spatial neglect and of task demands (implicit or explicit activation of the mental number line). Furthermore, it is interesting to note that the modulation of the numerical error by interval size was comparable to the one observed in the mental number line bisection task of Experiment 1.

4. Conclusions

In the present study, we investigated the relationship between numerical and visual space representations in right brain-damaged patients with or without joint deficits of space and numbers processing.

In Experiment 1, we showed that the rightward numerical bisection bias and left neglect have the same probability of occurring or not occurring together and, that, when both present, numerical bisection error and neglect severity are not significantly correlated. These results replicate and extend to a larger sample of patients ($N = 32$) the functional dissociation between visual and numerical bisection errors reported in previous single case or small group studies (Doricchi et al., 2009, 2005; Loetscher and Brugger, 2009; Rossetti et al., 2004; van Dijck et al., 2011). Recent anatomical data (Doricchi et al., 2009, 2005) have shown that the occurrence of numerical bisection errors follows damages outside brain areas typically associated with left unilateral neglect, namely subcortical and/or cortical structures at the level of the right prefrontal areas. In the present study, scans were not available for all patients, so we could not perform an analysis of lesion location. However, it is worth noticing that medical reports indicated that thirteen D+ patients (out of eighteen) had lesions involving frontal areas whereas twelve D− patients (out of fourteen) had lesions not involving frontal areas (see Table 1).

In Experiment 2, we demonstrated that when visual and numerical spatial representations are co-activated in a visual–numerical bisection task, only the numerical error is modulated by interval size (not the spatial error). The absence of a distance effect on the spatial error argues against the existence of a continuous and spatially organized numerical representation. Our results are consistent with data on healthy participants showing that the numerical distance between flanker numbers does not affect spatial biases (de Hevia et al., 2006). These findings challenge the idea that numerical and physical space share the same representational metric (Umilta et al., 2009; Zorzi et al., 2006) since they show that when both numerical and visual space representations are co-activated they do not influence each other.

Summing up, our experiments showed that, although neglect in visual and numerical space can co-occur, they are dissociable and that visual and numerical spatial representations are independent when co-activated. This, in turn, supports the notion that the visuospatial operations required to navigate along numerical and visual space are distinct neurocognitive mechanisms (Ashkenazi and Henik, 2010; Doricchi et al., 2009, 2005; Loetscher and Brugger, 2009; Loetscher et al., 2009; Rossetti et al., 2004; Tian et al., 2011; van Dijck et al., 2011; van Dijck et al., 2012).

If the representation of numerical magnitudes has, at least partially, different spatial attributes from the representation of physical space, what is its exact nature? Although there is not yet a definite answer to this question, a possible interpretation of the mental number line effect that has been recently advanced (Doricchi et al., 2009, 2005; van Dijck et al., 2011) argues that it might arise from the inability to construct or retain an active representation of the initial part of the number intervals on the mental number line. Hence, effective position-based verbal working memory might be crucial for normally performing numerical tasks that are thought to involve spatial representations of numerical magnitudes. Our results cannot directly confirm this interpretation because data on spatial working memory deficits were not available for the entire sample of patients. Nonetheless, we consider such a hypothesis very interesting but, at the same time, worth of further investigation [indeed, not all spatial–numerical interactions can be explained by working memory impairments (Fischer et al., 2003)]. Finally, we acknowledge that our results should be taken with caution because they are based mainly on negative results and that further studies are needed in order to better clarify the nature of the representation of numerical magnitudes as well as its anatomo–functional relationship with space representation.

Acknowledgments

These works was in part supported by a PRIN grant to Lorenzo Pia, Marco Neppi-Modona and Alessia Folegatti.

References

Ashkenazi S and Henik A. A disassociation between physical and mental number bisection in developmental dyscalculia. Neuropsychologia, 48(10): 2861e2868, 2010.

Bartolomeo P, Thiebaut de Schotten M, and Doricchi F. Left unilateral neglect as a disconnection syndrome. Cerebral Cortex, 17(11): 2479e2490, 2007.

Bisiach E and Vallar G. Unilateral neglect in humans. In Boller F, Grafman J, and Rizzolatti G (Eds), Handbook of Neuropsychology. Amsterdam: Elsevier Science, 2000: 459e502.

Bonato M, Priftis K, Marenzi R, and Zorzi M. Modulation of hemispatial neglect by directional and numerical cues in the line bisection task. Neuropsychologia, 46(2): 426e433, 2008.

Cappelletti M, Freeman ED, and Cipolotti L. The middle house or the middle floor: Bisecting horizontal and vertical mental number lines in neglect. Neuropsychologia, 45(13): 2989e3000, 2007.

Chatterjee A. Cross-over, completion and confabulation in unilateral spatial neglect. Brain, 118: 455e465, 1995.

de Hevia MD, Girelli L, and Vallar G. Numbers and space: A cognitive illusion? Experimental Brain Research, 168(1e2): 254e264, 2006.

Dehaene S, Bossini S, and Giraux P. The mental representation of parity and number magnitude. Journal of Experimental Psychology, 122(3): 371e396, 1993.

Dehaene S, Piazza M, Pinel P, and Cohen L. Three parietal circuits for number processing. Cognitive Neuropsychology, 20(3e6): 487e506, 2003.

Diller L and Weinberg J. Hemi-inattention in rehabilitation: The evolution of a rational remediation program. Advances in Neurology, 18: 63e82, 1977.

Doricchi F, Guariglia P, Gasparini M, and Tomaiuolo F. Dissociation between physical and mental number line bisection in right hemisphere brain damage. Nature Neuroscience, 8(12): 1663e1665, 2005.

Doricchi F, Merola S, Aiello M, Guariglia P, Bruschini M, Gevers W, et al. Spatial orienting biases in the decimal numeral ystem. Current Biology, 19(8): 1e6, 2009.

Fischer MH, Castel AD, Dodd MD, and Pratt J. Perceiving numbers causes spatial shifts of attention. Nature Neuroscience, 6(6): 555e556, 2003.

Hubbard EM, Piazza M, Pinel P, and Dehaene S. Interactions between number and space in parietal cortex. Nature Reviews Neuroscience, 6(6): 435e448, 2005.

Loetscher T and Brugger P. Random number generation in neglect patients reveals enhanced response stereotypy, but no neglect in number space. Neuropsychologia, 47(1): 276e279, 2009.

Loetscher T, Nicholls ME, Towse JN, Bradshaw JL, and Brugger P. Lucky numbers: Spatial neglect affects physical, but not representational, choices in a Lotto task. Cortex, 46(5): 685e690, 2009.

Pia L, Corazzini LL, Folegatti A, Gindri P, and Cauda F. Mental number line disruption in a right-neglect patient after a left-hemisphere stroke. Brain and Cognition, 69(1): 81e88, 2009.

Pizzamiglio L, Judica A, Razzano C, and Zoccolotti P. Toward a comprehensive diagnosis of visual-spatial disorders in unilateral brain damaged patients. Psychological Assesment, 5: 199e218, 1989.

Priftis K, Zorzi M, Meneghello F, Marenzi R, and Umilta C. Explicit versus implicit processing of representational space in neglect: Dissociations in accessing the mental number line. Journal of Cognitive Neuroscience, 18(4): 680e688, 2006.

Rossetti Y, Jacquin-Courtois S, Rode G, Ota H, Michel C, and Boisson D. Does action make the link between number and space representation? Visuo-manual adaptation improves number bisection in unilateral neglect. Psychological Science, 15(6): 426e430, 2004.

Tian Y, Wei L, Wang C, Chen H, Jin S, Wang Y, et al. Dissociation between visual line bisection and mental number line bisection in schizophrenia. Neuroscience Letters, 491(3): 192e195, 2011.

Umilta C, Priftis K, and Zorzi M. The spatial representation of numbers: Evidence from neglect and pseudoneglect. Experimental Brain Research, 192(3): 561e569, 2009.

van Dijck JP, Gevers W, Lafosse C, Doricchi F, and Fias W. Non- spatial neglect for the mental number line. Neuropsychologia, 49(9): 2570e2583, 2011.

van Dijck JP, Gevers W, Lafosse C, and Fias W. The heterogeneous nature of numberespace interactions. Frontiers in Human Neuoroscience, 5: 182, 2012.

Zamarian L, Egger C, and Delazer M. The mental representation of ordered sequences in visual neglect. Cortex, 43(4): 542e550, 2007.

Zorzi M, Priftis K, Meneghello F, Marenzi R, and Umilta C. The spatial representation of numerical and non-numerical sequences: Evidence from neglect. Neuropsychologia, 44(7): 1061e1067, 2006.

Zorzi M, Priftis K, and Umilta` C. Brain damage: Neglect disrupts the mental number line. Nature, 417(6885): 138e139, 2002.