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Causal role of spatial attention in arithmetic problem solving: Evidence from left unilateral neglect

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ABSTRACT

Recent behavioural and brain imaging studies have provided evidence for rightward and leftward attention shifts while solving addition and subtraction problems respectively, suggesting that mental arithmetic makes use of mechanisms akin to those underlying spatial attention. However, this hypothesis mainly relies on correlative data and the causal relevance of spatial attention for mental arithmetic remains unclear. In order to test whether the mechanisms underlying spatial attention are necessary to perform arithmetic operations, we compared the performance of right brain-lesioned patients, with and without left unilateral neglect, and healthy controls in addition and subtraction of two-digit numbers. We predicted that patients with left unilateral neglect would be selectively impaired in the subtraction task while being unimpaired in the addition task. The results showed that neglect patients made more errors than the two other groups to subtract large numbers, whereas they were still able to solve large addition problems matched for difficulty and magnitude of the answer. This finding demonstrates a causal relationship between the ability to attend the left side of space and the solving of large subtraction problems. A plausible account is that attention shifts help localizing the position of the answer on a spatial continuum while subtracting large numbers.

1. Introduction

Highly advanced human cognitive abilities, such as reading or solving arithmetical problems, are mainly learned by cultural transmission. Because these abilities are too recent in human evolution to benefit from a predefined brain representation, it has been proposed that cultural transmission exploits pre-existing mechanisms in the sensory-motor system to ensure their development (Andres, Michaux, & Pesenti, 2012; De Cruz, 2006; Dehaene & Cohen, 2007).

A widespread view assumes that the mental representation of numbers relies on a visuospatial medium, conceptualized as an imaginary line where numbers are represented from left to right in an ascending order (Restle, 1970). Unilateral spatial neglect provides a direct test for this assumption since this disorder affects the ability to attend to the contralesional hemispace, leading to ipsilesional biases not only in the physical (for a review, see Halligan, Fink, Marshall, & Vallar, 2003) but also in the representational space (e.g., Bisiach & Luzzatti, 1978; Rode, Rossetti, & Boisson, 2001). On the one hand, several results show that patients with left unilateral neglect shift the midpoint of a numerical interval toward large numbers in mental bisection tasks (Cappelletti, Freeman, & Cipolotti, 2007; Doricchi, Guariglia, Gasparini, & Tomaiuolo, 2005; Doricchi et al., 2009; Hoeckner et al., 2008; Loftus, Nicholls, Mattingley, & Bradshaw, 2008; Pia, Corazzini, Folegatti, Gindri, & Cauda, 2009; Priftis, Zorzi, Meneghello, Marenzi, & Umiltà, 2006; van Dijck, Gevers, Lafosse, & Fias, 2012; Zamarian, Egger, & Delazer, 2007; Zorzi, Priftis, & Umiltà, 2002; for a review, see Umiltà, Priftis, & Zorzi, 2009). This bias toward large numbers was interpreted as reflecting an inability to attend to the left end of a spatial continuum where numbers are represented in ascending order (Zorzi et al., 2002). Other results questioned the idea of a functional isomorphism in neglect patients between the representation of number and space in long-term memory, suggesting that biases in mental bisection of numerical intervals could arise from defective spatial working memory (Aiello et al., 2012; Aiello, Merola, & Doricchi, 2013; Doricchi et al., 2005, 2009; Pia et al., 2012; Rossetti et al., 2011) that might impair the encoding and maintenance of numbers while the patients perform the task (van Dijck, Gevers, Lafosse, Doricchi, & Fias, 2011). The important role of working memory mechanisms in number-space interactions was

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corroborated by several studies in healthy participants (Fias, van Dijck, & Gevers, 2011; Gevers et al., 2010; van Dijck & Fias, 2011; van Dijck, Abrahamse, Majerus, & Fias, 2013).

On the other hand, the performance of neglect patients in number comparison tasks suggests that their difficulties to process numbers on a spatial continuum may differ according to task demands: patients take more time to judge the magnitude of numbers immediately preceding the standard of comparison irrespective of its actual magnitude (e.g., when asked to compare numbers to a standard reference of 5, the patients were slower to respond to 4 than to 6, while they were slower to respond to 6 than to 8 when the reference was 7; Masson, Pesenti, & Dormal, 2013; van Dijck et al., 2012; Vuilleumier, Ortigue, & Brugger, 2004). Hence, the difficulties of neglect patients in the comparison task can be explained by the requirement to shift attention leftward relative to a reference rather than by the absolute position of numbers on a spatial continuum (Vuilleumier et al., 2004).

Mental arithmetic offers an interesting framework to test current views on number–space interactions since subtracting or adding a number can be viewed as shifting attention leftward or rightward on a spatial continuum (Hubbard, Piazza, Pinel, & Dehaene, 2005). Indeed, stimulus-response compatibility effects have shown that subtraction induces leftward attention shifts whereas addition induces rightward attention shifts (Knops, Viarouge, & Dehaene, 2009a; Wiemers, Bekkering, & Lindemann, 2014; Masson & Pesenti, 2014; Pinhas & Fischer, 2008). Several studies also reported a tendency to underestimate the results of subtraction problems and to overestimate the results of addition problems (Knops et al., 2009a; Knops, Thirion, Hubbard, Michel, & Dehaene, 2009b; Lindemann & Tira, 2011; McCrink, Dehaene, & Dehaene-Lambertz, 2007; McCrink & Wynn, 2009), which is reminiscent of a phenomenon known as *representational momentum* that arises from the use of spatial functions to anticipate the position of a moving target (Finke & Freyd, 1985). It is worth noting that other interpretations of the *operational momentum* effect have been proposed (i.e., the compression interpretation, McCrink et al., 2007; Chen & Verguts, 2012). A functional magnetic resonance Imaging (fMRI) study further showed that the parietal circuits involved in eye movements partially overlap with those involved in calculation (Knops et al., 2009b). However, these correlative data are not sufficient to establish a causal link between spatial attention and exact calculation as attention shifts may go along with arithmetic problem solving without being necessary to it.

In order to overcome this limitation, the present study investigates arithmetic performance in neglect patients. So far, calculation difficulties have never been reported in neglect patients, presumably because the standard arithmetic tests used in previous studies were limited to a few simple problems (e.g., Rossetti et al., 2004; Zorzi et al., 2002). In the present study, we measured the performance of right brain-lesioned patients, with or without left spatial neglect, and of healthy controls in closely matched subtraction and addition problems. Different predictions can be made concerning the performance of left neglect patients, depending on whether one considers that the involvement of spatial attention is determined by the absolute position of numbers on a spatial continuum or by their position relative to each other. If the role of spatial attention is determined by the absolute position of the operands and answer on a left-to-right oriented continuum, neglect patients should experience more difficulties to solve arithmetic problems with small numbers because, whatever the operation (i.e., addition or subtraction), these are located on the left side of the putative continuum. On the contrary, if the role of spatial attention is determined by the position of the answer relative to the position of the first operand, left neglect patients should experience more difficulties in the subtraction task than in the addition task because subtraction would require shifting attention to the left of the first operand, whereas addition would not. In order to take into account the possible role of working memory in mediating the relationship between spatial and numerical abilities, we also measured the general ability of patients to hold spatial and verbal sequences in short-term memory.

Table 1
Clinical and demographic characteristics of patient groups.

Patients	Gender	Age (years)	Aetiology	Time from lesion (months)	Lesion site
With neglect (N+)					
1	F	46	Ischemic	2.5	R Fronto-Parietal
2	M	48	Haemorrhagic	2.5	R Capsulo-Thalamic
3	F	59	Haemorrhagic	6	R Parietal
4	M	59	Ischemic	9	R Fronto-Parietal
5	M	53	Haemorrhagic	1	R Temporo-Parietal
6	M	58	Haemorrhagic	16	R Fronto-Temporo-Parietal
7	M	51	Ischemic	9	R Fronto-Parietal
8	M	42	Ischemic	6	R Fronto-Parietal
9	F	45	Ischemic	1.5	R Temporo-Parietal
10	F	47	Haemorrhagic	2	R Temporo-Parietal
11	F	63	Ischemic	1.5	R Fronto-Parietal
12	F	57	Ischemic + Haemorrhagic	3	R Temporo-Parietal
13	F	49	Haemorrhagic	3	R Fronto-Temporo-Parietal
14	M	61	Ischemic	2.5	R Fronto-Parietal
Without neglect (N−)					
1	F	46	Haemorrhagic	10	R Temporo-Parietal
2	M	69	Ischemic + Haemorrhagic	3	R Capsulo-Thalamic
3	M	34	Ischemic + Haemorrhagic	3	R Capsulo-Thalamic + Parietal
4	M	54	Ischemic	22.5	R Temporo-Parietal
5	M	79	Ischemic	7	R Temporo-Parietal
6	M	37	Haemorrhagic	3	R Thalamic
7	M	42	Haemorrhagic	5	R Fronto-Parietal
8	F	29	Ischemic	3	R Fronto-Temporo- Parietal
9	M	69	Ischemic	17	R Temporo-Parietal
10	M	59	Ischemic	22	R Fronto-Parietal

F: female, M: male; R: right.

Table 2
Summary of the patients' scores at the neuropsychological assessment.

Patients	**BIT subtests**						**TAP Neglect subtest**		**Verbal span**		**Visuo-spatial span**
With neglect (N+)	*Line crossing* (*cut-off*=34)	*Letter cancellation* (*cut-off*=32)	*Star cancellation* (*cut-off*=51)	*Figures and shapes copy* (*Cut-off*=3)	*Line Bisection* (*cut-off*=7)	*Representational drawing* (*cut-off*=2)	*Left omissions*	*Right omissions*	*Forward*	*Backward*	*Forward*
1	30[a]	27[a]	44[a]	1[a]	7	1[a]	20	4	6	4	3
2	36	30[a]	50[a]	3	6[a]	1[a]	14	6	6	2	3
3	36	27[a]	43[a]	4	9	1[a]	17	10	4	2	4
4	36	31[a]	49[a]	1[a]	3[a]	0[a]	21	6	6	3	5
5	36	34	51	1[a]	9	1[a]	12	7	5	3	6
6	33[a]	33	42[a]	1[a]	0[a]	1[a]	21	3	6	5	4
7	14[a]	9[a]	9[a]	0[a]	3[a]	0[a]	21	14	4	2	0
8	3[a]	36	50[a]	3	5[a]	1[a]	22	9	7	3	3
9	36	31[a]	46[a]	3	9	2	11	3	5	3	6
10	36	13[a]	15[a]	0[a]	2[a]	1[a]	22	13	5	3	4
11	36	11[a]	15[a]	0[a]	2[a]	0[a]	/	/	6	3	4
12	17[a]	20[a]	32[a]	2[a]	0[a]	1[a]	21	11	5	4	3
13	12[a]	16[a]	22[a]	1[a]	6[a]	0[a]	/	/	5	4	6
14	17[a]	8[a]	4[a]	0[a]	0[a]	0[a]	/	/	5	3	2
Without neglect (N−)											
1	36	40	53	4	6[a]	3	8	7	5	4	6
2	36	40	54	3	9	3	0	0	4	3	6
3	36	40	54	4	9	3	0	1	5	3	4
4	36	36	49[a]	3	9	2	6	9	5	3	4
5	36	38	53	4	9	3	0	1	4	3	5
6	36	40	54	4	9	3	0	2	5	5	5
7	36	37	50	4	9	2	0	1	4	2	6
8	36	40	54	4	9	3	1	1	4	3	6
9	35	40	54	4	9	3	3	0	6	4	5
10	36	40	54	4	9	3	5	0	6	4	4

Span: maximum length.
/: Test not achievable.
Note that three patients were unable to realize the neglect subtest of the TAP due to their motor impairment.

[a] Below the cut-off.

2. Methods

2.1. Participants

The study was conducted at the National Center for Functional Reeducation and Readaptation (Rehazenter) in Luxembourg with 24 patients who had suffered right-hemisphere brain lesions at least one month before testing. The patients gave their written informed consent to participate in the study, which was conducted in accordance with the principles stated in the Declaration of Helsinki. Demographical and clinical details are listed in Tables 1 and 2. They were right-handed, and had normal or corrected-to-normal vision. Fourteen patients had left unilateral spatial neglect (N+ group; 7 females) and ten patients showed no spatial neglect (N− group; 2 females). The two groups of patients were matched according to demographical and clinical criteria (e.g., mean age: N+ $=53\pm6.7$ years; N− $=52\pm16.9$; $t(22)=0.184$, *ns*; time elapsed from lesions: N+ $=4.7\pm4.2$; N− $=9.5\pm8.0$; $t(22)=1.943$, *ns*; lesion site: presence of frontal, temporal, parietal and thalamic lesions in both groups of patients). The presence of unilateral spatial neglect was assessed through the *Behavioural Inattention Test* (BIT; Wilson, Cockburn, & Halligan, 1987; see below for more methodological details) and through the computerized neglect subtask of the *Test of Attentional Performance* (TAP; Zimmermann & Fimm, 2002). A patient was included in the N+ group if (a) she/he showed a score beyond the cut-off for at least two subtests of the BIT and (b) she/he showed symptoms of left-sided neglect in the TAP neglect subtest (see Table 2 for score details). We also measured the performance of fourteen age-matched healthy controls in the arithmetic tasks (HC group; seven females, mean age: 53 ± 6.3 years; mean age differences: [N+/HC]: $t(26)=0.231$, *ns*; [N−/HC]: $t(22)=0.302$, *ns*).

2.2. Neglect assessment

2.2.1. BIT subtests

The paper-and-pencil subtests of the BIT (Wilson et al., 1987) performed by the patients consisted of six of the most commonly used tests for assessing visual and representational neglect. The cut-off criteria reported in Table 2 correspond to the normative data provided for each subtest (see Robertson & Halligan, 1999).

2.2.1.1. Line crossing test. The patient had to cross out 40 black 2.5 cm long lines printed on an A4 sheet. No distractor stimulus was displayed on the sheet. The score was the number of lines crossed out in the left and right parts of the sheet.

2.2.1.2. Letter/star cancellation tests. The patient had to search for and cross out target symbols (i.e., two specific letters or a small star respectively) among distractor symbols (i.e., other letters or other letters and larger stars respectively) on an A4 sheet. Patients with left unilateral neglect typically fail to cancel stimuli on the left side of the sheet. The score corresponded to the number of symbols that the patient crossed out.

2.2.1.3. Figure copying test. The patient had to copy four hand-drawing figures: a flower, a star, a cube, and geometric shapes (i.e., four different triangles). Each figure received 1 point if the copy matched the model and 0 if it was incomplete or spatially incorrect.

2.2.1.4. Line bisection test. The patient had to indicate the midpoint of three lines of 20 cm displayed horizontally on the same A4 sheet placed in front of them in alignment with the body midline. The first line was presented on the right of the sheet, the second one was centrally displayed and the third was on the left part. The subtest is scored by measuring the deviation of the bisection mark from the actual midpoint of the line.

2.2.1.5. Free drawing test. The patient had to draw from memory a clock face, a man or a woman, and a butterfly on an A4 sheet. A score of 1 point was attributed to each drawing if the figure was complete and symmetric. This subtest is commonly used to assess representational neglect (Rode et al., 2001; Rossetti et al., 1998).

2.2.2. Neglect subtest of the TAP

In this computerized test (Zorzi et al., 2002), patients had to detect peripheral flickering targets (i.e., flickering three-digit numbers) appearing at random positions and random time intervals among steady distractors (i.e., two- or three-digit numbers) by pressing a key. To ensure central fixation, the patients had to read out each change of a centrally presented letter. The number of right and left omissions was computed to get further evidence for the presence or absence of left unilateral neglect (Table 2).

2.3. Tasks and procedure

Arithmetic performance was assessed in a single session within the two weeks that followed the neuropsychological examination of spatial neglect. We also measured the verbal (forward and backward) and visuospatial span of each patient in order to see whether differences between groups could be explained by working memory deficits. The testing of HC participants included the arithmetic task only.

2.3.1. Arithmetic task

The participants were asked to answer arithmetic problems on auditory presentation. Problems were defined as a function of the magnitude of the answer sampled across three different decades (i.e., small: 25, 26; medium: 54, 55; and large: 83, 84). In order to index the amplitude of attention shifts along the putative number line, problems also varied as a function of the magnitude of the second operand, classified as small (i.e., $n\pm1$, $n\pm2$), medium (i.e., $n\pm6$, $n\pm7$) or large (i.e., $n\pm11$, $n\pm12$). In total, the combination of the six answers and six operands led to a list of 36 addition and 36 subtraction problems (Table 3). To prevent participants from memorizing the answer of arithmetic problems after repeated presentation, a second list of problems was created by changing the sign of the 36 addition and subtraction problems of the first list (i.e., addition became subtraction and vice versa); these problems were used as fillers and were not included in the analyses.

Stimulus presentation and data collection were controlled by a laptop using the E-prime software (Schneider, Eschman, & Zuccolotto, 2000). Addition and subtraction problems were played out of the laptop speakers. At the beginning of each trial, a fixation cross was displayed for 500 ms, at the centre of the computer screen (17″), in black on a white background. An arithmetic problem was then played for a duration ranging from 1 to 3 s and a question mark was displayed at the centre of the screen until the participant's response. The participants were asked to say aloud the answer; response latencies (RL) were recorded using a voice key and corresponded to the time between the stimulus offset and the verbal response as detected by the voice key; response accuracy was monitored on-line by the experimenter who also controlled the presentation of the next trial by pressing the space bar to make sure that the response was correctly recorded and that the patient was focused on the task. The experiment was composed of 4 blocks of 72 trials so that each problem was presented twice. In each block, addition and subtraction problems were played in a random order.

Table 3
List of addition and subtraction problems as a function of the magnitude of the second operand (small, medium or large) and the magnitude of the answer (small, medium or large).

Second operand	*Answer*	*Addition*	*Subtraction*
Small	*Small*	24+1=25	26−1=25
		25+1=26	27−1=26
		23+2=25	27−2=25
		24+2=26	28−2=26
	Medium	53+1=54	55−1=54
		54+1=55	56−1=55
		52+2=54	56−2=54
		53+2=55	57−2=55
	Large	82+1=83	84−1=83
		83+1=84	85−1=84
		81+2=83	85−2=83
		82+2=84	86−2=84
Medium	*Small*	19+6=25	31−6=25
		20+6=26	32−6=26
		18+7=25	32−7=25
		19+7=26	33−7=26
	Medium	49+6=54	60−6=54
		49+6=55	61−6=55
		47+7=54	61−7=54
		48+7=55	62−7=55
	Large	77+6=83	89−6=83
		78+6=84	90−6=84
		76+7=83	90−7=83
		77+7=84	91−7=84
Large	*Small*	14+11=25	36−11=25
		15+11=26	37−11=26
		13+12=25	37−12=25
		14+12=26	38−12=26
	Medium	43+11=54	65−11=54
		44+11=55	66−11=55
		42+12=54	66−12=54
		43+12=55	67−12=55
	Large	72+11=83	94−11=83
		73+11=84	95−11=84
		71+12=83	95−12=83
		72+12=84	96−12=84

2.3.2. Working memory

The functioning of the verbal and visuospatial working memory was evaluated by means of the forward and backward digit spans and the block tapping test (WMS-III; Wechsler, 1997). The latter test was administered in the ipsilesional space of the N+ patients.

2.4. Data analysis

For each combination of operation, answer and second operand, we computed the individual error rate (ER) and the average response latency (RL) for correct trials. These values were entered in separate analyses of variance (ANOVAs) with operation (addition vs. subtraction), answer (small, medium vs. large) and second operand (small, medium vs. large) as within-subject variables, and group (N+, N− vs. HC) as a between-subject variable. Given the low error rate in some conditions, the average magnitude of the error (i.e., the difference between the erroneous and the correct answers) was computed for each task after collapsing the data across levels of answer and second operand.

The ANOVA modeled all main effects and all interactions including group and/or operation. We aimed to test the hypothesis of a selective deficit for subtraction by evidencing (i) an interaction between operation and group; (ii) an increased ER in subtraction compared to addition in N+ only; (iii) and a significant difference between N+ and the two control groups in the subtraction task only. *Post-hoc* comparisons were performed using one-tailed *t*-tests ($p<0.05$) adjusted for multiple comparisons using Bonferroni correction.

3. Results

3.1. Mental arithmetic

3.1.1. Errors analyses

A main effect of group ($F(2,35)=15.582$, $p<0.001$, $\eta^2=.47$) showed that the ER was higher in N+ (mean ER ± S.D.: 8.78 ± 4.76%) than in HC (1.98 ± 1.05%; $t(26)=5.215$, $p<0.002$) but not than in N− (5.69 ± 2.47%; $t(22)=1.869$, *ns*); moreover, N− made significantly more errors than HC ($t(22)=5.056$, $p<0.03$). A main effect of answer ($F(2,70)=10.756$, $p<0.001$, $\eta^2=.24$) indicated that the ER for small answers (3.30 ± 3.51%) was lower than the ER for medium (6.14 ± 5.51%; $t(37)=3.760$, $p<0.003$) and large (7.01 ± 6.17%; $t(37)=4.567$, $p<0.001$) answers; no difference was observed between problems with medium and large answers ($p>0.05$). There was also a main effect of second operand ($F(2,70)=16.643$, $p<0.001$, $\eta^2=.32$): participants made less errors when they added or subtracted small numbers (1.88 ± 4.08%) compared to medium (7.03 ± 6.25%; $t(37)=4.712$, $p<0.001$) or large (7.54 ± 6.88%; $t(37)=4.299$, $p<0.001$) numbers; no difference was observed between problems with medium and large second operands ($p>0.05$). The significant two-way interactions between operation and group ($F(2,35)=6.781$, $p<0.004$, $\eta^2=.28$) and between second operand and group ($F(4,70)=2.522$, $p<0.05$, $\eta^2=.13$) were qualified by a three-way interaction between second operand, operation and group ($F(4,70)=2.982$, $p<0.03$, $\eta^2=.15$). To decompose this latter interaction, we looked at the interaction between group and operation as a function of the magnitude of the second operand.

When the second operand was large (Fig. 1A), we found a main effect of operation ($F(1,35)=7.324$, $p<0.02$, $\eta^2=.17$), showing that subtraction problems (10.08 ± 7.97%) induced more errors than addition problems (5.00 ± 6.11%), and a main effect of group ($F(2,35)=9.275$, $p<0.001$, $\eta^2=.35$), showing that HC (2.53 ± 4.33%) made less errors than N+ (11.76 ± 10.76%; $t(26)=4.05$, $p<0.001$) and N− (8.33 ± 6.03%; $t(22)=3.874$, $p<0.004$), whereas no difference was found between N+ and N− ($t(22)=1.193$, *ns*). operation and group interacted with each other ($F(2,35)=7.692$, $p<0.003$, $\eta^2=.31$): N+ made more errors in the subtraction (19.35 ± 14.58%) than in the addition (4.17 ± 6.93%; $t(13)=3.536$, $p<0.006$) task, whereas no difference was observed between tasks in N− (7.92 ± 4.59% vs. 8.75 ± 7.47%, $t(9)=0.327$, *ns*) and HC (2.98 ± 4.74 vs. 2.08 ± 3.92, $t(13)=0.479$, *ns*). Further *post-hoc* comparisons showed that, when they were asked to subtract large numbers, N+ made significantly more errors than HC ($t(26)=3.994$, $p<0.005$) and N− ($t(22)=2.382$, $p<0.04$); a significant difference was also found between N− and HC ($t(22)=2.550$, $p<0.05$). In contrast, when they were asked to add large numbers, N+ did not differ from N− and HC (all $p>0.1$); only N− made more errors than HC ($t(22)=2.852$, $p<0.03$). When the second operand was medium (Fig. 1B), we found a main effect of operation ($F(1,35)=5.831$, $p<0.03$, $\eta^2=.143$), the addition task (8.99 ± 8.11%) giving rise to more errors than the subtraction task (5.08 ± 4.43%). A main effect of group ($F(2,35)=10.124$, $p<0.001$, $\eta^2=.37$) showed that HC (2.38 ± 2.81%) performed better than N+ (11.01 ± 6.56%; $t(26)=4.525$, $p<0.001$) and N− (7.71 ± 5.29%; $t(22)=3.203$, $p<0.005$), irrespective to the arithmetic operation; the two groups of patients did not differ from each other ($t(22)=1.314$, *ns*). No interaction was found for this condition ($F<1$). When the second operand was small (Fig. 1C), we found neither a main effect of operation ($F(1,35)=3.358$, *ns*) or group ($F(2,35)=1.771$, *ns*) nor any interaction ($F(2,35)=2.779$, *ns*).

The analysis of error rate did not reveal any other significant main effect or interaction (all $p>0.1$).

The analysis of the relative magnitude of errors revealed no significant main effect of group ($F(2,35)=2.06$, *ns*) or operation ($F(1,35)=0.342$, *ns*) and no interaction between these variables ($F(2,35)=0.361$, *ns*).

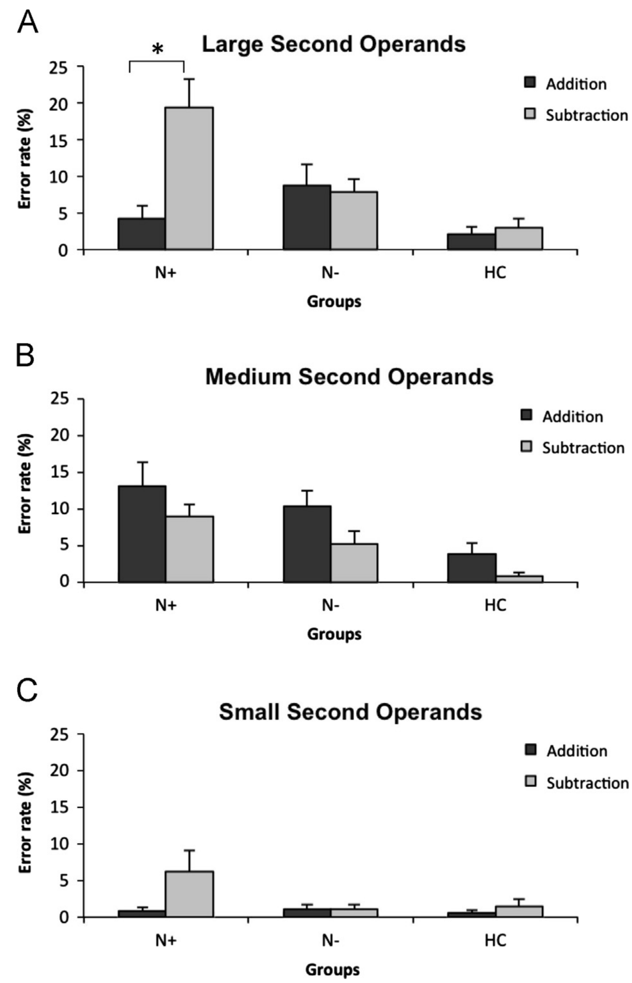

Fig. 1. Mean error rate (±S.E.) for the group of patients with (N+) and without left unilateral spatial neglect (N−) and healthy controls (HC), as a function of the operation (Subtraction vs. Addition) and the magnitude of the second operand, classified as small (i.e., 1,2), medium, (i.e., 6,7) or large (i.e., 11,12). Asterisks indicate significant differences between the two arithmetic operations ($p<0.05$).

3.1.2. Response latencies analysis

A main effect of GROUP ($F(2,35)=12.682$, $p<0.001$, $\eta^2=.42$) showed that N+ (mean RL ± S.D.: 2899 ± 1630 ms) were slower than HC (833 ± 409 ms; $t(26)=4.601$, $p<0.001$) but not than N− (1750 ± 720 ms; $t(22)=2.079$, *ns*); a RL difference was also found between HC and N− ($t(22)=3.972$, $p<0.004$). Main effects of ANSWER ($F(2,70)=38.458$, $p<0.001$, $\eta^2=.52$) and SECOND OPERAND were also observed ($F(2,70)=28.213$, $p<0.001$, $\eta^2=.45$): RLs increased with the magnitude of the answer (small: 1527 ± 1178 ms; medium: 1863 ± 1474 ms; large: 2116 ± 1559 ms; small/medium: $t(37)=-4.369$, $p<0.001$; medium/large: $t(37)=-4.480$, $p<0.001$) and with the magnitude of the second operand (small: 1265 ± 986 ms; medium: 1875 ± 1394 ms; large: 2366 ± 1970 ms; small/medium: $t(37)=-5.461$, $p<0.001$; medium/large: $t(37)=-5.069$, $p<0.001$). The two-way interactions between ANSWER and GROUP ($F(4,70)=38.458$, $p<0.003$, $\eta^2=.22$) and between SECOND OPERAND and GROUP ($F(4,70)=6.951$, $p<0.001$, $\eta^2=.28$) were qualified by a three-way interaction between SECOND OPERAND, ANSWER and GROUP ($F(8,140)=2.327$, $p<0.03$, $\eta^2=.12$).

When the second operand was large, we found a main effect of GROUP ($F(2,35)=13.308$, $p<0.001$, $\eta^2=.43$), showing that N+ (3945 ± 2339 ms; $t(26)=4.603$, $p<0.001$) and N− (2075 ± 874 ms; $t(22)=3.789$, $p<0.003$) were slower than HC (997 ± 539 ms) whereas no difference was found between N+ and N− ($t(22)=2.398$, *ns*). There was also a main effect of ANSWER ($F(2,70)=35.194$, $p<0.001$, $\eta^2=.50$), showing that large answers (2756 ± 2302 ms; $t(37)=6.067$, $p<0.001$) and medium answers (2605 ± 2154 ms; $t(37)=5.661$, $p<0.001$) took more time to be computed than small answers (1740 ± 1574 ms); no difference was found between large and medium answers ($t(37)=1.521$, *ns*). Moreover, a GROUP by ANSWER interaction ($F(4,70)=4.409$, $p<0.003$, $\eta^2=.20$) showed that N+ (small: 3001 ± 1943 ms, medium: 4302 ± 2537 ms, large: 4531 ± 2736 ms) and N− (small: 1333 ± 576 ms, medium: 2351 ± 1074 ms, large: 2543 ± 1174 ms) responded slower than HC for each magnitude of the answer (small: 769 ± 429 ms, medium: 1088 ± 575 ms, large: 1132 ± 613 ms; all $p<0.001$). A difference was found between the RLs of N+ and N− only when the answer was small ($t(22)=2.619$, $p<0.05$) but not when it was medium or large (all $p<0.1$).

When the second operand was medium, we found a main effect of GROUP ($F(2,35)=10.452$, $p<0.001$, $\eta^2=.38$), showing that N+ (2842 ± 1661 ms; $t(26)=4.261$, $p<0.001$) and N− (1911 ± 852 ms; $t(22)=3.850$, $p<0.004$) were slower than HC (883 ± 449 ms) whereas no difference was found between N+ and N− ($t(22)=1.620$, *ns*). There was also a main effect of ANSWER ($F(2,70)=19.550$, $p<0.001$, $\eta^2=.36$), showing that large answers (2203 ± 1516 ms) took more time to be computed than medium (1788 ± 1521 ms; $t(37)=4.415$, $p<0.001$) and small answers (1633 ± 1262 ms; $t(37)=6.025$, $p<0.001$) whereas small and medium answers did not differ from each other ($t(37)=1.422$, *ns*). Moreover, a GROUP by ANSWER interaction ($F(4,70)=3.101$, $p<0.03$, $\eta^2=.15$) showed that N+ (small: 2411 ± 1570 ms, medium: 2792 ± 1929 ms, large: 3322 ± 1665 ms) responded slower than HC for each magnitude of the answer (small: 785 ± 343 ms, medium: 860 ± 542 ms, large: 1003 ± 503 ms; all $p<.001$), whereas their RLs did not differ from those of N− (small: 1733 ± 863 ms, medium: 1682 ± 893 ms, large: 2318 ± 936 ms; all $p>0.1$). A difference was found between the RLs of HC and N− when the answer was small or large (all $p<0.004$) but not when it was medium ($t(22)=2.809$, *ns*).

When the second operand was small, we found a main effect of GROUP ($F(2,35)=8.418$, $p<0.002$, $\eta^2=.33$) showing that HC (620 ± 305 ms) answered faster than N+ (1911 ± 1247 ms; $t(26)=3.772$; $p<0.004$) and N− (1264 ± 571 ms; $t(22)=3.617$, $p<0.01$); no difference was found between the two groups of patients ($t(22)=1.524$, *ns*). A main effect of ANSWER was also observed ($F(2,70)=4.541$, $p<0.02$, $\eta^2=.12$): problems with medium answer (1197 ± 975 ms) were processed faster than problems with large answer (1389 ± 1247 ms; $t(37)=3.169$, $p<0.01$), while no difference was observed between other categories (all p-values >0.1). There was no significant interaction between the two factors ($F(4,70)=0.535$, *ns*).

Importantly, the analysis of RLs revealed no main effect of OPERATION ($F(1,35)=0.286$, *ns*) and no interaction between OPERATION and GROUP ($F(2,35)=0.413$, *ns*). There were no other significant three-way or four-way interactions (all $p>0.05$).

3.2. Working memory

No difference was observed between N+ and N− groups for the forward digit span (mean span level ± S.D. for N+: 5.36 ± 0.84; N−: 4.80 ± 0.79; $t(22)=1.640$, $p>0.1$) and for the backward digit span (N+: 3.14 ± 0.86; N−: 3.40 ± 0.84; $t(22)=0.726$, *ns*). For the visuospatial span, N+ (3.79 ± 1.67) showed a lower score than N− (5.10 ± 0.88; $t(22)=2.264$, $p<0.04$).

4. Discussion

A growing body of evidence from behavioural and brain imaging studies suggests that arithmetic problem solving involves mechanisms akin to those underlying spatial attention orientation (Andres, Pelgrims, Michaux, Olivier, & Pesenti, 2011; Knops et al., 2009a,b; Lindemann & Tira, 2011; Masson & Pesenti, 2014; McCrink et al., 2007; Pinhas & Fischer, 2008). Indeed, the solving of addition and subtraction problems has been associated respectively with right and left attention shifts in healthy participants. However, the causal role of spatial attention in mental arithmetic has never been established so far. In order to address this issue, we compared the performance of right brain-lesioned patients, with (N+) and without (N−) left unilateral neglect, and healthy controls (HC) while they solved subtraction and addition problems. If the involvement of spatial attention is determined by the absolute position of the numbers on a spatial continuum, an interaction between group and answer magnitude should be observed regardless of the type of operations. On the contrary, if the role of spatial attention is related to the position of the answer relative to the first operand, an interaction between group and operation should be observed, such that the inability to attend the left side of space would impair subtraction but not addition of two-digit numbers regardless of which part of the numerical continuum is concerned.

The results showed that N+ made more errors (up to 20%) than HC and N− in the subtraction task, whereas they were as accurate in the addition task. The range of arithmetic problems cannot explain the selective deficit of N+ because subtraction and addition were closely matched for the magnitude of the answers and for the magnitude of the second operands. The performance of HC and N− showed that subtraction problems were solved as fast and as accurately as addition problems, meaning that the two arithmetic tasks were of equal difficulty for participants without neglect symptoms. N+ did not favour speed over accuracy in the subtraction task, compared to the addition task, as an increase in RLs was observed in both patient groups (i.e., N+ and N−) compared to the control group (i.e., HC), irrespective of the arithmetic operation, presumably because brain damage resulted in a general cognitive slowdown in patients.

Therefore, we argue that the distinct pattern of performance of N+ in the subtraction task is a direct consequence of left unilateral neglect. The present results converge with previous findings to show that interactions between mental arithmetic and spatial attention are bidirectional. Indeed, it was previously shown that computing the answer of arithmetic operations induces attention shifts (Knops et al., 2009a,b; Masson & Pesenti, 2014; Pinhas & Fischer, 2008). Here, we found that difficulties to attend the left side of space can hamper the solving of subtraction problems. So far, the interactions between spatial attention and mental arithmetic were based on correlative data from behavioural and brain imaging studies. Our results provide the first evidence of a causal relationship between spatial attention and mental arithmetic.

Interestingly, the impact of neglect on mental arithmetic was influenced by the magnitude of the second operand that was defined as small (i.e., 1 and 2), medium (i.e., 6 and 7) or large (i.e., 11 and 12). The results showed that N+ had no problem adding or subtracting 1 and 2 units, suggesting that spatial attention plays little or no role when solving small arithmetic problems or that N+ are not in trouble performing small amplitude attentional shifts. In contrast, N+ experienced more difficulties than N− and HC to subtract 11 or 12 units. A recent study suggested that patients with left unilateral neglect show a form of *object-based* neglect affecting the internal processing and integration of units and decades according to the place-value structure of the Arabic system, where the decade is represented leftward to the unit (Klein et al., 2013). Object-based neglect for two-digit number processing was characterized by an increased unit-decade compatibility effect: the comparison of two-digit numbers took more time when the units and decades point to opposite (e.g., 53 vs. 71) rather than similar (e.g., 53 vs. 31) responses, and by faster comparison of within-decade pairs (e.g., 53 vs. 58) than between-decade pairs (e.g., 53 vs. 45). In the present study, the difficulties of N+ while subtracting two-digit numbers cannot be explained by object-based neglect because such a deficit should also affect the solving of addition problems since they were matched with subtraction problems for difficulty and magnitude of the second operand. It is worth noting that neither subtraction nor addition problems with large second operands required borrowing procedures. The reason why object-based neglect for two-digit number processing did not affect accuracy in arithmetic tasks could simply be due to the use of oral number words, rather than Arabic digits, in both stimulus and response modalities. Finally, an increased ER was also observed in problems with medium second operands but it is worth noting that it was not modulated by arithmetic operation and observed in patients with and without neglect. We suggest that the increased ER observed in N+ and N− arises from the additional working memory load associated with arithmetic problem solving in this condition. Indeed, adding or subtracting medium operands, in contrast to small or large operands, involved carrying/borrowing procedures in most problems (8 out of 12 problems in each operation). Since both N+ and N− encountered difficulties with these particular problems, they cannot stem from neglect. It is reasonable to assume that patients had more difficulties than HC to apply carrying/borrowing procedures while adding or subtracting medium operands, because of mild impairment of executive functions after brain lesions.

According to a recent neurocomputational model, the solving of subtraction problems implies a left attention shift, after mapping the operands onto a left-to-right oriented continuum, because the answer is smaller and thus more leftward positioned than the first operand (Chen & Verguts, 2010, 2012). The data we collected in neglect patients indicate that the requirement to shift attention leftward relative to the first operand rather than the absolute spatial mapping of numbers is responsible for their difficulties in solving large subtraction problems. Indeed, the correct performance of N+ in the addition task irrespective of the magnitude of the answer suggests that they are still able to process numbers, to map them onto a mental continuum and to shift attention to the right side of this continuum since the answer of addition problems is always larger and thus located more rightward than the two operands. The absence of interaction with the magnitude of the answer indicates that the role of spatial attention in arithmetic operations is determined by the relative position of the answers with respect to the first operand (i.e., always smaller for subtraction and always larger for addition) rather than by their absolute position in a putative mental number line. The view that attention shifts are defined by the relative rather than absolute position of the numbers to be processed is further corroborated by the performance of neglect patients in standard number comparison tasks where a deficit to mentally orient their attention towards the representation of numbers located on the left side of a given reference number was observed whatever the magnitude of the reference (Masson et al., 2013; Vuilleumier et al., 2004).

Because left unilateral neglect did not interfere with the subtraction of small numbers (i.e., single-digit numbers), it is reasonable to assume that spatial attention is called into action mainly when larger numbers (i.e., two-digit numbers) are subtracted. We propose that, when the numerical range covered by arithmetic operations increases, attention shifts are involved to localize the position of the answer on a spatial continuum where numbers are mapped from left to right. It is unclear whether neglecting the left side of space would lead to an overestimation of the answer in the subtraction task, although this prediction seems plausible given the performance of N+ in mental bisection of numerical intervals (e.g., Cappelletti et al., 2007; Zorzi et al., 2002) and the existence of response biases, such as the *operational momentum*, in mental arithmetic (i.e., underestimation of subtraction results and overestimation of addition results; e.g., McCrink et al., 2007; Knops et al., 2009a). In the present study, left unilateral neglect led to greater imprecision in subtraction problem solving but the analysis of the relative magnitude of the errors did not reveal any difference between groups and operations. This aspect of arithmetic performance may be investigated using different tasks and/or a larger set of problems in order to refine the assessment of response biases in neglect. Because we were primarily interested in the causal role of spatial attention in exact arithmetic, we designed a task that required participants to say aloud the correct answer of subtraction and addition problems presented in a symbolic format. In contrast, the *operational momentum* effect is typically observed in tasks that require participants to approximate the result of subtraction and addition problems by selecting the closest number among a set that never contains the exact answer (McCrink et al., 2007; Knops et al., 2009a). These methodological discrepancies may account for the absence of significant response biases in the present study, especially if one considers that the *operational momentum* effect is dramatically reduced when problems are presented in a symbolic rather than a non-symbolic format (Knops et al., 2009a). Our results thus provide the first evidence of a causal relationship between spatial attention and mental arithmetic. In order to validate the hypothesis that arithmetic operations are analogue to shifting attention along a spatial continuum, future studies should look for the opposite pattern of performance in patients with right unilateral spatial neglect (i.e., impaired addition problem solving in the context of preserved subtraction problem solving). Although the present study was designed to match the two arithmetic operations in perceptual, numerical and response complexity, such evidence is needed to definitely exclude that non-spatial processes could account for the deficit of left neglect patients in the subtraction task.

While numerous recent neuropsychological studies investigated the consequence of spatial neglect on number processing, previous findings were limited to mental number interval bisection or comparison tasks (e.g., Vuilleumier et al., 2004; Zorzi et al., 2002). Here, we extended the role of attention orientation to mental arithmetic, which represents a more elaborate aspect of our mathematical skills. The question arises why the difficulties of neglect patients to solve arithmetic problems remained undetected in previous studies. First, in most studies, it is not possible to reach firm conclusions about the arithmetic skills of neglect patients simply because these are little documented as mental arithmetic was not the main focus of these studies (e.g., Rossetti et al., 2004; Zamarian et al., 2007; Zorzi et al., 2002). The testing was usually limited to a few arithmetic problems, often part of the neuropsychological examination, with little information about stimulus selection and modality of presentation. Second, none of the previous studies recorded RLs that can provide important information about the use of backup strategies or speed-accuracy trade-offs. Third, our results showed that the difficulties of neglect patients in mental arithmetic were rather selective, as they concerned only the subtraction of large numbers, so that they were likely to remain undetected without a systematic investigation of the effect of number magnitude across operations. To the best of our knowledge, despite growing evidence in the brain imaging literature, the interference of spatial attention with mental arithmetic was never discussed in former patient studies.

Previous findings pointed out that the performance of neglect patients in mental bisection of numerical intervals could be mediated by working memory deficits (Doricchi et al., 2005; Pia et al., 2012; van Dijck et al., 2011). Hence, in the sample tested by Doricchi et al. (2005), only patients with lesions in the prefrontal areas underlying working memory processes showed a rightward numerical bias, suggesting that the deviation in number interval bisection was the consequence of a working memory impairment rather than of neglect *per se*. A similar argument was brought by the recent single-case study of a left brain-lesioned patient who showed signs of spatial neglect for the right visual hemispace but left neglect for numbers (i.e., overestimation of the midpoint of number interval; van Dijck et al., 2011). The authors showed that, in this patient, the deviation in mental bisection of numerical intervals arose from a general deficit in processing the initial items of any ordered series in working memory. In order to test whether the effect of neglect on arithmetic performance is mediated by working memory deficits, we measured verbal and visuospatial memory spans in each patient. Results showed that N+ did not experience more difficulties than N− to recall verbal sequences from short-term memory either forward or backward. Consequently, our results support the idea that, at least in this sample of patients, the difficulties of N+ in subtraction are mediated by a visuospatial deficit rather than a verbal working memory deficit. The idea that numerical deficits can occur in neglect independently of verbal working memory impairment further fits with other studies involving number comparison tasks (Masson et al., 2013; Vuilleumier et al., 2004). Testing the visuospatial memory span revealed lower scores in N+ than N−, a result often observed in neglect patients (Malhotra, Mannan, Driver, & Husain, 2004; Wojciulik, Husain, Clarke, & Driver, 2001). An impairment of the visuospatial working memory does not seem sufficient to account for the arithmetic performance of N+ because defective visuospatial working memory is known to contribute to the severity of neglect in general (Malhotra et al., 2004) and because the difficulties of N+ to subtract two-digit numbers contrast with their preserved ability to add two-digit numbers, a task that recruit visuospatial working memory resources (Trbovich & LeFevre, 2003; Zago et al., 2008). We assume that the difficulties of N+ in visuospatial working memory are related to their spatial attention deficit. Neglect may have affected the encoding of spatial locations in the block tapping test, although the setup was positioned in ipsilesional space, or it may have affected the processing of the working memory content itself. Several brain imaging studies have indeed demonstrated a functional and anatomical overlap between the neural substrate of visuospatial working memory (Wager & Smith, 2003), attention orientation (Beauchamp, Petit, Ellmore, Ingeholm, & Haxby, 2001), and spatial mental imagery (Mellet, Petit, Denis, & Tzourio, 1998). In the present study, impaired visuospatial working memory could possibly have exacerbated arithmetic difficulties, but they could not account for them independently of neglect. More generally, our finding adds to the view that the contribution of working memory to number-space interactions is not the same for all numerical tasks (van Dijck et al., 2012). A mapping study of the lesions responsible for the deficits observed in patients might help drawing distinctions between the cognitive processes responsible for the numerical deficits of neglect patients, as previously illustrated by the association of biases in mental bisection of numerical intervals with lesions of working memory prefrontal structures (Doricchi et al., 2005).

5. Conclusion

Patients with left unilateral spatial neglect experienced selective difficulties to solve subtraction problems compared to addition problems closely matched for difficulty and magnitude of the answer and second operand. These results support the hypothesis that arithmetic operations involve attention shifts to localize the position of the answer on a spatial continuum. Our data corroborate the view that attention shifts are defined by the relative rather than absolute position of the numbers to be processed. In the present study, the involvement of attention shifts was evidenced for the subtraction of large numbers, suggesting that the role of attention shifts is related to approximating the answer when the spatial distance between the first operand and the answer is large. In order to validate this hypothesis, future studies should gather evidence for selective difficulties with addition problem solving in patients with right unilateral spatial neglect while controlling the solving strategy used by patients.

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