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Shifts of Spatial Attention Underlie Numerical Comparison and Mental Arithmetic: Evidence From a Patient With Right Unilateral Neglect

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Objectives: Recent findings suggest that mental arithmetic involves shifting attention on a mental continuum in which numbers would be ordered from left to right, from small to large numbers, with addition and subtraction causing rightward or leftward shifts, respectively. Neuropsychological data showing that brain-damaged patients with left neglect experience difficulties in solving subtraction but not addition problems support this hypothesis. However, the reverse dissociation is needed to establish the causal role of spatial attention in mental arithmetic. ***Method:*** R.H., a 65-year-old left-brain-damaged patient exhibiting right unilateral visuospatial and representational neglect, was tested with various numerical tasks including numerical comparison, arithmetic problem-solving, and numerical interval bisection. ***Results:*** In numerical comparison, R.H. showed a selective response latency increase when judging numbers larger than the references whereas his performance was normal for numbers smaller than the references. In the arithmetic task, R.H. was impaired in solving addition but not subtraction problems. In contrast, performance in number bisection shows a deviation toward larger numbers. ***Conclusion:*** These results establish a double dissociation between subtraction and addition solving in patients with left versus right neglect and demonstrate clear evidence that attentional mechanisms are crucial for mental arithmetic. We suggest that attention shifts are involved whenever a number is represented relative to another on a mental continuum, be it during numerical comparison or arithmetic problem-solving. R.H.'s performance in numerical interval bisection indicates that this task involves processes that are distinct from those involved in number comparison and mental arithmetic.

General Scientific Summary
The involvement of attentional mechanisms in arithmetic problem-solving was tested in a left brain-lesioned patient with right neglect. The patient was slower to compare numbers larger than standard references and was specifically more impaired in solving addition problems than subtraction problems. The results reveal an inverted pattern of impairment between subtraction and addition in right compared with left neglect and show the critical implication of spatial attention in arithmetic.

Keywords: numerical processing, arithmetic, neglect, spatial attention, double dissociation

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It has been suggested that numbers are represented spatially along a mental continuum, with smaller numbers on the left and larger numbers on the right (Dehaene, 1992). Accordingly, processing large numbers orients attention to the right side of space whereas processing small numbers orients attention to the left side of space (e.g., Casarotti, Michielin, Zorzi, & Umiltà, 2007; Di

Luca, Pesenti, Vallar, & Girelli, 2013; Fischer, Castel, Dodd, & Pratt, 2003; Fischer, Warlop, Hill, & Fias, 2004). Moreover, when asked to fixate a central visual stimulus, merely listening to small or large numbers induces leftward or rightward ocular drifts, respectively (Myachykov, Ellis, Cangelosi, & Fischer, 2016). The manipulation of spatial attention is also found to influence participants' response latencies (RLs) in numerical comparison to a fixed standard: numbers larger than the standard are responded to faster when presented in the right hemifield and numbers smaller than the standard are responded to faster when presented in the left hemifield (Lavidor, Brinksman, & Göbel, 2004). Inducing reflexive eye movements with optokinetic stimulation (OKS) has been shown to affect numerical processing in a numerical comparison task: rightward OKS facilitated the processing of large numbers whereas leftward OKS did not have such an effect on small number processing (Ranzini et al., 2015). This was also found when participants had to make voluntary eye movements (smooth pursuit and saccades) to the right (Ranzini, Lisi, & Zorzi, 2016). Moreover, left-sided cues delayed the processing of large numbers and right-sided cues delayed the processing of small numbers (Kramer, Stoianov, Umiltà, & Zorzi, 2011; Stoianov, Kramer, Umiltà, & Zorzi, 2008). These findings suggest that attention orientation supports the mental manipulation of numbers on a visuospatial medium. In this view, solving subtraction and addition problems may be analogous to shifting attention respectively leftward and rightward along a mental continuum. Several studies in healthy children and adult participants reported a tendency to overestimate the results of addition problems and underestimate the results of subtraction problems (Knops, Dehaene, Berteletti, & Zorzi, 2014; Knops, Viarouge, & Dehaene, 2009b; Knops, Zitzmann, & McCrink, 2013; Lindemann & Tira, 2011; McCrink, Dehaene, & Dehaene-Lambertz, 2007; McCrink & Wynn, 2009; Pinhas & Fischer, 2008). This bias has mostly been interpreted as reflecting a representational momentum characterized by an attentional move that would go too far along the mental continuum (for a review, see Hubbard, 2014, 2015). Recently, it has been shown that solving addition or subtraction problems causes attentional shifts to the right or to the left, respectively (e.g., Hartmann, Mast, & Fischer, 2016; Marghetis, Nunez, & Bergen, 2014; Masson & Pesenti, 2014; Pinhas & Fischer, 2008; Werner & Raab, 2014). Moreover, presenting the second operand on the right side of the screen facilitated the solving of additions whereas presenting the second operand on the left side of the screen facilitated the solving of subtractions (Mathieu, Gourjon, Couderc, Thévenot, & Prado, 2016). Conversely, Masson and Pesenti (2016) showed that flickering distractors presented during the solving of arithmetic problems had a greater interfering effect if they were presented on the side of space where attention was supposed to have been directed. Subtraction solving orienting attention toward the left side of space and addition solving toward the right side of space, left-sided flickering distractors interfered more with subtraction problems whereas right-sided targets interfered more with addition problems. It is worth noting that the distractors were presented 300 msec after the second operand had been presented and lasted for 900 msec. The mean RL being approximately 2,500 msec for both additions and subtractions, this paradigm ensured that the distractors were interfering with the solving step and not merely with the processing of the second operand or with the production of the answer. This showed that attention orientation actually took place

during the solving process and was not a mere byproduct of it. It is interesting to note that activations elicited by addition problem-solving partially overlap with the activations elicited by rightward saccades in the posterior superior parietal lobule (PSPL; Knops, Thirion, Hubbard, Michel, & Dehaene, 2009a), suggesting that addition problem-solving shares some neural bases with attention orientation.

Neuropsychological studies in neglect patients suggest further causal evidence for the recruitment of attentional mechanisms during number processing. Neglect is characterized by an inability to attend to the contralesional hemispace (Heilman, 1979) and an attentional deviation that biases the bisection of physical lines toward ipsilesional space (Halligan, Fink, Marshall, & Vallar, 2003). Although left unilateral neglect after a right hemispheric lesion is far more frequent, right unilateral neglect is sometimes observed after a left hemispheric lesion (Stone, Halligan, & Greenwood, 1993). In addition to the physical misperception of space, neglect may also affect the contralesional side of mentally generated images (i.e., representational neglect; e.g., Bisiach & Luzzatti, 1978; Bisiach, Pizzamiglio, Nico, & Antonucci, 1996; for a recent review, see Salvato, Sedda, & Bottini, 2014). However, several studies report a double dissociation between neglect for physical and representational space, suggesting that perceptual spatial attention shifts and imaginal spatial attention shifts rely on mechanisms that are at least partially distinct (e.g., Guariglia, Palermo, Piccardi, Iaria, & Incoccia, 2013; Piccardi, Bianchini, Zompanti, & Guariglia, 2008). Patients who exhibit representational neglect fail to report the contralesional side of well-known places (Bisiach & Luzzatti, 1978), of geographic maps (Rode, Perenin, & Boisson, 1995), of mentally reconstructed stimuli such as cloud-like/geometrical shapes (Bisiach, Nichelli, & Sala, 1979; Ogden, 1985), or o'clock faces (Grossi, Angelini, Pecchinenda, & Pizzamiglio, 1993; Grossi, Modafferi, Pelosi, & Trojano, 1989).

Spatial biases in processing numbers have been investigated in neglect patients mainly with three tasks: numerical interval bisection, number comparison, and arithmetic problem-solving. When asked to indicate the midpoint of a numerical interval, left neglect patients misplaced their answer toward larger numbers (Zorzi, Priftis, & Umiltà, 2002). This bias was replicated in several studies and was interpreted as an inability to attend to the left part of the mental number line (e.g., Cappelletti, Freeman, & Cipolotti, 2007; Hoeckner et al., 2008; Priftis, Pitteri, Meneghello, Umiltà, & Zorzi, 2012; Zamarian, Egger, & Delazer, 2007; Zorzi, Priftis, Meneghello, Marenzi, & Umiltà, 2006). A right neglect patient was reported to exhibit a bias toward smaller numbers, suggesting that the failure to orient attention to the neglected side was responsible for the observed numerical distortion in numerical interval bisection (Pia, Corazzini, Folegatti, Gindri, & Cauda, 2009). This bias toward smaller numbers was later observed in a group of right brain-lesioned patients (Woodbridge, Chechlacz, Humphreys, & Demeyere, 2013). Moreover, in left neglect patients, inducing visuospatial shifts of attention to the left either by having them wear shifting prisms (Rossetti et al., 2004) or by administering them leftward OKS (Priftis et al., 2012) reduced their overestimation bias. Some studies showed that the more severe the neglect, the greater the overestimation bias in numerical interval bisection (Pitteri, Kerkhoff, Keller, Meneghello, & Priftis, 2015; Yang, Tian, & Wang, 2009). However, a double dissociation between physical line and numerical interval bisection has also been re-

ported in left neglect patients (Doricchi, Guariglia, Gasparini, & Tomaiuolo, 2005; Pia et al., 2012; Storer & Demeyere, 2014; Woodbridge et al., 2009). Indeed, not all left neglect patients showed a numerical impairment and, conversely, some right brain-lesioned patients without neglect showed a spatial-numerical bias during mental bisection of number intervals. Moreover, a single case study of a right neglect patient showed a rightward bias for numerical interval bisection, which is the pattern of responses classically showed by left neglect patients (van Dijck, Gevers, Lafosse, Doricchi, & Fias, 2011). The authors of this study suggested that biases in numerical interval bisection might rather be the consequence of working memory impairment because patients may fail to encode and maintain the sequence of numbers while performing the task. It is important to note that most studies investigating numerical biases in neglect patients did not test whether patients showed representational neglect. Some authors stressed that line bisection is performed in physical space whereas numerical interval bisection is performed in imaginal space (Pitteri et al., 2015; Zorzi et al., 2012). They suggested that the physical space representation and number representation might be functionally isomorphic because they share similar properties while being distinct representations. Crucially, most studies investigating numerical interval bisection did not test whether the patients had impairments for navigating into imaginal space. Because physical neglect does not always come along with representational neglect, it is likely that some neglect patients did not show a bias in numerical interval bisection because their neglect did not extend to mental space.

In comparison-to-a-standard tasks, participants have to classify a given number as smaller or larger than a standard number. Results show that left neglect patients are abnormally slow to process the number just smaller than the reference (Masson, Pesenti, & Dormal, 2013, 2016a; Salillas, Granà, Juncadella, Rico, & Semenza, 2009; van Dijck, Gevers, Lafosse, & Fias, 2012; Vuilleumier, Ortigue, & Brugger, 2004; Zorzi et al., 2012). When asked to compare numbers to 5, left neglect patients were slower to respond to 4 than to 6, but when asked to compare numbers to 7, they were slower to respond to 6 than to 8 (Vuilleumier et al., 2004). The fact that the impairment observed in left neglect patients was not dependent on the magnitude of the number to process but varied as a function of the standard used in the task implies that left neglect does not alter the representation of small numbers per se but causes an impairment in accessing or in orienting attention to the left side of the mental representation of numbers relative to the standard.

Finally, the assessment of arithmetic abilities in a group of left neglect patients revealed a specific impairment in subtraction solving whereas addition solving was preserved (Dormal, Schuller, Nihoul, Pesenti, & Andres, 2014). This deficit was present irrespective of the magnitude of the response, suggesting that left neglect actually hampers the ability to shift attention leftward to the first operand of subtraction problems to localize the correct response along a left-to-right oriented continuum. In this view, the attentional mechanisms underlying arithmetic problem-solving would be similar to those recruited in comparison tasks for accessing the representation of the target relative to the standard.

It is worth noting that previous studies did not consider the possibility that comparison and mental arithmetic tasks could show a similar pattern of impaired performance as a consequence of spatial attention disorders. So far, predictions about the role of spatial attention in mental arithmetic have only been tested in patients with left neglect (Dormal et al., 2014). Moreover, previous results have shown a dissociation between impaired subtraction and preserved addition in left neglect patients, but the reverse dissociation is still awaited. Thus, careful examination of numerical and arithmetic skills in a right neglect patient is crucial (a) to test whether the same attention mechanisms explains deficits in number comparison, numerical interval bisection, and mental arithmetic and (b) to establish the causal role of attention orientation in these tasks. The present study investigates the numerical and arithmetic performances of R.H., a patient showing clear signs of right neglect both in the perceptual and representational domains. If attentional shifts are crucial to performing the aforementioned numerical tasks, then R.H. should show a pattern of response opposite to the one observed in left neglect patients in past studies because of his impairment in orienting attention to the right: a deviation toward smaller numbers in numerical interval bisection, higher RLs for processing numbers larger than the standard compared with numbers smaller than the standard in a comparison task, and a greater impairment in solving addition but not subtraction problems. A different pattern of performance in one or several of these numerical tasks would suggest that the numerical biases previously observed in left neglect patients may not all derive from a deficit in attention orientation. Because it has been suggested that spatial numerical biases in left neglect could be the consequence of an impairment for encoding and maintaining the sequence of numbers (e.g., van Dijck et al., 2011), we also examined the working memory abilities of R.H.

Case Report

R.H. is a 65-year-old man and a former interior architect with a postgraduate degree. He had no previous neurological or psychiatric history. In November 2013, he was admitted to an emergency ward for sudden right hemiplegia. Magnetic resonance (MR) examination revealed a rupture of a cerebral abscess located in the left parieto-occipital junction causing a subdural empyema along the cerebral falx extending to the anterior part of the frontal lobe and the inferior part of the temporal lobe (Figure 1 and online supplemental material) that necessitated surgical drainage. Approximately 9 months later, MR images showed a complete regression of the subdural empyema and the persistence of a parasagittal parieto-occipital lesion (Figure 2 and online supplemental material). Fluid-attenuated inversion-recovery (FLAIR) T2-weighted images further showed a residual spot of hypersignal in the left occipital and another in the left anterior frontal white matter, with small increase of the apparent diffusion coefficient (ADC) value that might suggest mild demyelination in these areas (see Figure 2). During his hospitalization, R.H. showed clinical signs of right neglect consisting in head and gaze deviation to the left, which was confirmed by standard neuropsychological evaluation in April 2014. The patient did not show any sign of aphasia before and after surgery.

The present investigation took place between April 2014 and September 2014 and received the approval of the local ethical committee. R.H. gave his informed consent to participate in this study as required by the Declaration of Helsinki. R.H. was able to organize his agenda to schedule the testing sessions without inter-
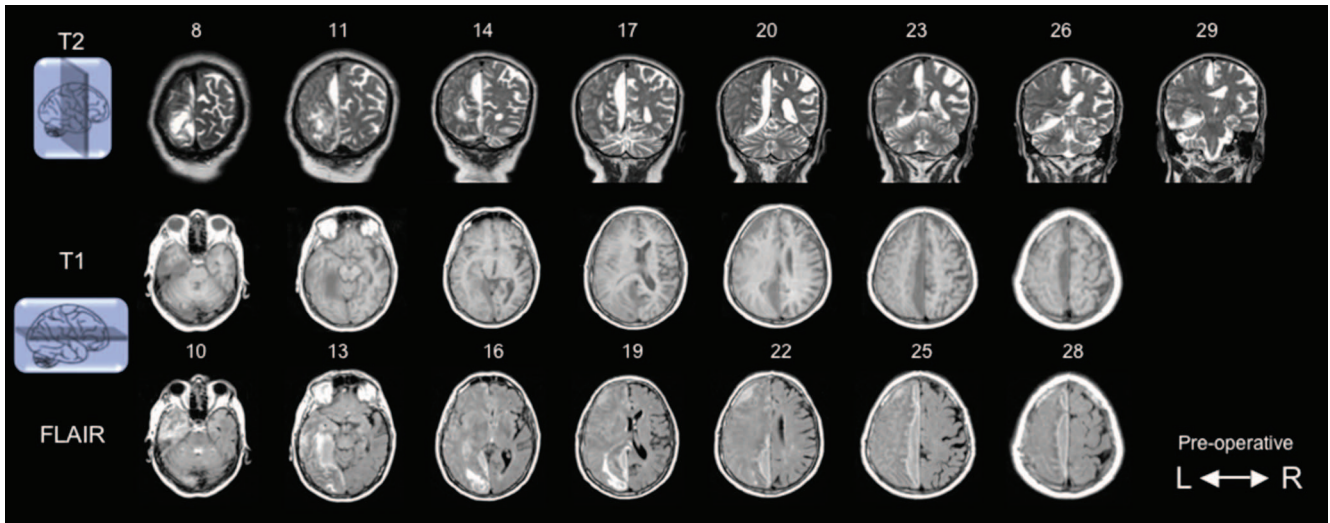
Figure 1. R.H., a 65-year-old patient, had a surgical drainage after a rupture of a cerebral abscess. Preoperative T2-weighted (up; coronal view), T1-weighted (middle; axial view), and FLAIR (down; axial view) MR images showing the presence of an abscess situated at the parieto-occipital junction. The subsequent subdural empyema was located along the cerebral falx and extended to the inferior part of the temporal lobe and to the anterior part of the frontal lobe. Data are shown in native space in neurological convention (left-is-left). See the online article for the color version of this figure.

fering with his revalidation program at the hospital. Performance in standardized neglect tests (Physical line bisection and Neglect subtest of Test for Attention Performance [TAP]) was assessed by comparison to the available norms whereas performance in the other tasks was directly compared to a healthy control group (hereafter HC) composed of male participants with no neurological or psychiatric history who were matched for age and educational level. Depending on the task, the HC group contained seven to nine participants that gave written consent to participate. Crawford and Howell's (1998) modified t test that allows a single test score obtained from an individual to be compared to the performance of a small control sample was used for testing whether R.H. was impaired in the following tasks in comparison to HC. Crawford and Garthwaite's (2005) Revised Standardized Difference Test (RSDT) was used for assessing whether the discrepancy between two conditions of one task was significantly different from the discrepancy observed in the HC. Thus, the RSDT assesses the presence of a dissociation by comparing the difference between

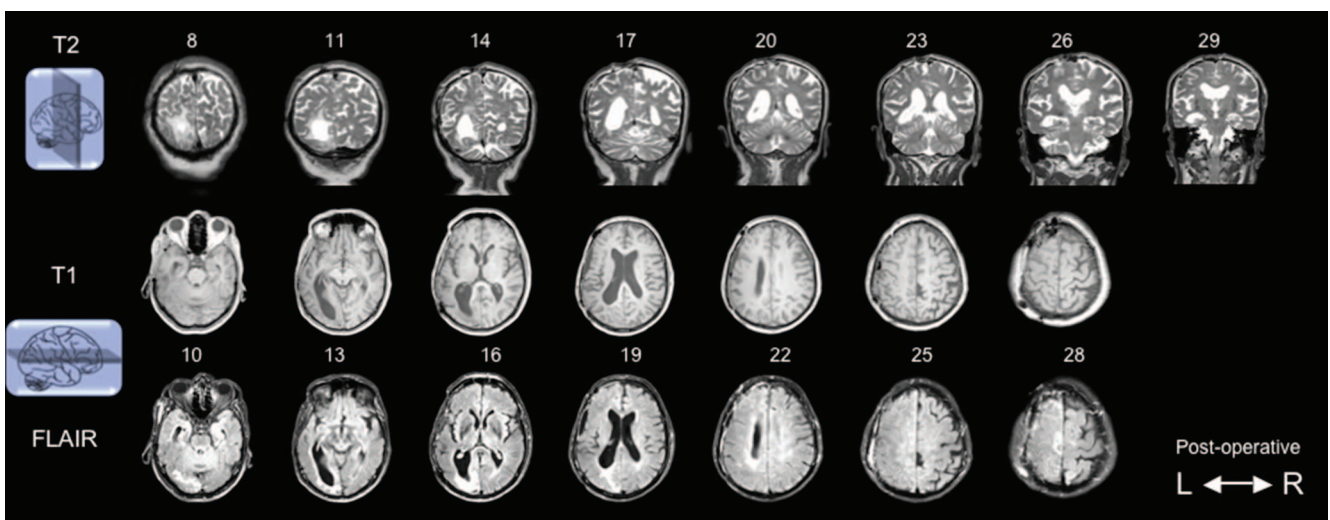*Figure 2.* R.H.'s postoperative T2- (up; coronal view) and T1-weighted (middle; axial view) MR images showing the residual parasagittal medial occipital lesion. FLAIR images (down, axial view) show residual spots of hypersignal in the left occipital and the left anterior frontal white matter. Data are shown in native space in neurological convention (left-is-left). See the online article for the color version of this figure.

two tasks for an individual with the distribution of differences in a control group.

Neglect Assessment

Perceptual visual neglect.

Physical line bisection (Azouvi et al., 2006). R.H. was asked to indicate the midpoint of an individually printed line of 20 cm length, presented centrally on an A4 horizontal sheet. A deviation of 6.5 mm and more indicates the presence of visual neglect. R.H. showed a leftward deviation of 11 mm suggesting the presence of right neglect.

The Bells Test (Gauthier, Dehaut, & Joanette, 1989). The Bells Test requires the patient to search and cross out all of the targets (i.e., bells) among various distractors on an A4 sheet. Three or more omissions indicate an attentional deficit. R.H. started with the left side of the sheet and omitted three right-sided targets, one left-sided target, and one central target.

Neglect subtest of TAP (Zimmermann & Fimm, 1995). In this computerized test, R.H. was asked to detect peripheral flickering targets (i.e., three-digit numbers) appearing at random positions on a 17-in. computer screen and at random time intervals among steady distractors (two- or three-digit numbers) by pressing a central response key while reading out loud centrally presented letters to ensure central fixation. The number of right and left omissions was computed and compared to assess the presence of neglect. R.H. omitted 72.7% of the targets located on the right and only 4.5% of the targets located on the left. This asymmetric number of omissions toward the right is interpreted as a sign of right visual neglect.

Representational neglect.

The O'Clock test (adapted from Grossi et al., 1993). R.H. and HC ($n = 7$) were asked to imagine pairs of clock faces corresponding to orally presented hours and to report in which one the hands of the clock made the largest angle. The test included 40 trials. In half of the trials, the hands of the clocks were located in the right part and in the other half of the trials they were located in the left part of the imagined clocks. R.H. responded correctly to 65% of the trials for pairs with the hands on the right and to 80% of the trials for pairs with the hands on the left. His performance was impaired for right side trials in comparison to the HC ($95 \pm 6.32\%$; $t(6) = 4.44$, $p = .004$) but not for left side trials ($92.5 \pm 6.89\%$; $t(6) = 1.697$, $p = .141$). To investigate the left–right asymmetry of R.H.'s performance, a laterality quotient (LQ) was computed (Piccardi et al., 2008) with the following formula: (*Left Accuracy – Right Accuracy*)/ *Left Accuracy + Right Accuracy*). A positive LQ indicates more errors when the hands are located on the right side of the clock and a negative LQ indicates more errors when the hands are located on the left side of the clock. R.H.'s LQ was 10.345, which was significantly larger than the HC's LQ (-1.351 ± 3.69; $t(6) = 2.965$, $p = .013$) and suggested that right neglect also occurred for his representational space.

R.H. and HC also performed a task in which they had to imagine a clock face corresponding to an orally presented hour and to indicate whether the hands formed an angle inferior or superior to 90° (e.g., inferior: 2:15; superior: 1:25; adapted from Kukolja, Marshall, & Fink, 2006). The test included 40 different trials, half with both hands on the left side and half with both hands on the right. R.H. responded correctly to 65% of the right trials and to 85% of the left trials. His performance was different from the HC for right ($96.67 \pm 4.08\%$; $t(6) = 7.261$, $p < .001$) but not for left trials ($95 \pm 6.32\%$; $t(6) = 1.48$, *ns*). R.H.'s LQ (13.333) was significantly larger than the HC's LQ (-0.927 ± 1.436; $t(6) = 9.289$, $p < .001$), which confirmed the presence of right representational neglect.

Working Memory Assessment

Forward and backward digit span. Working memory was assessed using the digit span tasks from the Weschler Adult Intelligence Scale (WAIS-III; Wechsler, 1997). R.H. and seven HC participants were orally given sets of digits they had to repeat forward or backward. R.H. had a forward digit span of 5 and a backward digit span of 4. In comparison to HC, R.H. showed no global deficit in this task (forward: 6 ± 1.0; $t(6) = 0.935$, $p = .38$; backward: 5.25 ± 1.11, $t(6) = 1.087$, $p = .31$).

Probe recognition task. Six randomly selected consonants were presented sequentially in the center of the screen for 1,000 msec, with a 500-msec blank interval between each letter. Participants were asked to read aloud these letters and to memorize them. After a retention interval of 2,000 msec, a probe letter appeared in the center of the screen and participants had to tell whether or not the letter was part of the memorized sequence. To avoid strategies based on visual shape information, the letters of the sequence were black and in uppercase whereas the probe letter was blue and in lowercase. Each position of the sequence was probed 2 times in three separated blocks. The task was composed of 72 trials; in half of the trials, the probe was not part of the sequence. No time constraint was given to answer. To examine position-based deficits in verbal working memory that would be characterized by an unequal distribution of mnemonic efficiency between the first and last items of the sequence to be retained, the data of the first and last half of the sequence were separately analyzed. R.H. correctly recognized 33.33% of the start elements, which was significantly inferior to the performance of the HC ($83.33 \pm 17.56\%$; $t(7) = 2.663$, $p = .037$). For the end elements, the performance of R.H. was 83.33%, which did not significantly differ from the HC ($95.23 \pm 5.94\%$; $t(7) = 1.877$, $p = .11$). Finally, no difference was found in rejecting new elements that were not part of the sequence (R.H.: 94.44%; HC: $93.55 \pm 6.55\%$; $t(7) = .113$, $p = .913$).

Basic Numerical Skills Assessment

Counting. R.H. and HC ($n = 9$) participants were asked to count forward from 1 to 31 and backward from 22 to 1. Both R.H. and HC performed without flaw.

Parity judgment. R.H. and HC ($n = 9$) participants had to tell whether 22 Arabic numbers ranging from 4 to 871 were odd or even. Both R.H. and HC performed without flaw.

Writing Arabic numerals under dictation. The experimenter read aloud 17 numbers ranging from 4 to 50,000. R.H. and HC ($n = 9$) participants had to write them in Arabic notation. R.H. and HC participants did not make any mistake in this task.

Experimental Tasks

Numerical Comparison

Method. Three blocks of numerical comparison were administered. In each block, R.H. and nine HC participants had to decide whether the stimulus was smaller or larger than a reference number by pressing a left or a right response key, respectively. The three blocks used a different standard of comparison (i.e., 4, 5, or 6) and were presented in a random order to each HC at the same session. R.H. performed the three tasks in different sessions on separate days. All participants responded with their right index and their right middle finger. The choice not to reverse the response mapping was motivated by previous studies using comparison paradigms with neglect patients that showed no effect of response mapping but showed that brain-lesioned patients had greater difficulty in switching a previously learned response mapping to a new response mapping (Vuilleumier et al., 2004). Digits ranged from a distance of 1 to 3 from the standard. For instance, when performing comparisons to 5, digits ranged from 2 to 8. Each block was composed of 72 trials (i.e., three blocks of 24 trials) corresponding to 12 repetitions of each item and began with 6 training trials that were not included in the analyses. The training aimed at ensuring that the participants had understood the instructions and had in mind the standard of comparison they had to refer to. Participants were instructed to respond as fast and accurately as possible. Each trial began with the presentation of a central fixation point to ensure that participants were fixating the center of the screen. Stimuli were 20-mm-high Arabic digits centrally presented for 400 msec in white on a black background.

Results. R.H. globally made 2.31% of errors, which was significantly different from the HC who made 0.93% of errors, $t(8) = 18.587$, $p < .001$; no other analysis was conducted because of the small overall error rate. The median RLs for correct answers for each digit were computed for each participant. R.H. was globally slower than HC when comparing digits to 4, ($t(8) = 3.913$, $p = .006$); to 5 ($t(8) = 5.207$; $p = .001$); and to 6 ($t(8) = 4.146$, $p = .002$). In comparison to 5, R.H. was slower than the HC 5 for digit 6 (840 msec; HC: 520 ± 59 msec; $t(7) = 5.114$, $p < .001$) and for digit 4 (732 msec; HC: 560 ± 65 msec; $t(7) = 2.495$, $p = .041$). The discrepancy between R.H.'s responses to 4 and 6 was significantly larger than the one observed in the HC ($t(7) = 2.982$, $p = .02$). For comparison to 6, R.H. was slower than the HC for responding to digit 7 (1,037 msec; HC: 563 ± 75 msec; $t(7) = 5.959$, $p < .001$) but not for responding to digit 5 (865 msec; HC: 674 ± 110 msec; $t(7) = 1.637$, $p = .145$). The RSDT showed that R.H. exhibited a discrepancy significantly larger than the HC between digit 7 and digit 5 ($t(7) = 3.251$, $p = .014$). For comparison to 4, R.H. was slower than the HC for digit 5 (908 msec; HC: 557 ± 121 msec; $t(7) = 2.735$, $p = .029$) and digit 3 (777 msec; HC: 555 ± 69 msec; $t(7) = 3.033$, $p = .019$). Although statistical analyses did not confirm that the discrepancy between R.H.'s response to digits 5 and 3 was significantly larger than in the HC ($t(7) = 0.332$, $p = .749$), in comparison to 4, the pattern was identical with the one observed in comparison to the standard 5 and 6 (see Figure 3).
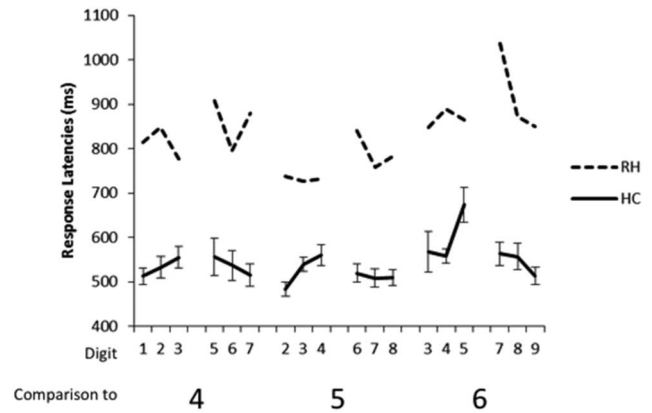

Figure 3. Mean RLs ($\pm SE$) in comparison to the standards 4, 5, and 6, respectively, for R.H. and HC as a function of the digit to be compared.

Arithmetic Task

Method. R.H. and nine HC participants were asked to answer arithmetic problems aloud on auditory presentation. The list of arithmetic problems was taken from Dormal et al. (2014) and contained 36 additions and 36 subtractions with six different answers and six different second operands. The magnitude of the answers (small: 25 and 26; medium: 54 and 55; large: 83 and 84) and of the second operands (small: 1 and 2; medium: 7 and 8; large: 11 and 12) were matched across operations. To prevent participants from memorizing the answers, the problems previously described were mixed with a filler list that was not included in the analyses. Fillers were created by changing the sign of the 72 addition and subtraction problems previously described (i.e., addition became subtraction and vice versa). Each problem was presented twice so that the experiment was composed of six blocks of 48 trials. Response accuracy was monitored online by the experimenter.

Results. For subtraction problems, R.H. made 18.06% of errors, which was significantly worse than HC ($1.85 \pm 1.96\%$; $t(8) = 7.846$, $p < .001$). For addition problems, R.H. made 30.56% of errors, which was also significantly worse than HC ($2.47 \pm 2.17\%$; $t(8) = 12.28$, $p < .001$). It is important to note that the difference between the error rates of R.H. in addition and subtraction was significantly larger than the difference between the error rates measured in the HC (RSDT, $t(8) = 2.384$, $p = .044$; Figure 4). These findings reveal a strong dissociation between addition and subtraction, indicating that R.H. showed more difficulties in solving addition problems compared with subtraction problems.

Number Interval Bisection

Method. R.H. and seven HC participants were instructed to state the midpoint between two orally presented numbers without making any calculation. Forty-eight number pairs were constructed following the method described by Zorzi et al. (2002). Number pairs were presented either in ascending or descending order in separate blocks. The length of the intervals to be bisected could be 3, 5, 7, or 9. Numbers ranged from 1 to 29 and each interval was presented using the units (i.e., 1–9), the teens (i.e., 11–19), or the twenties (i.e., 21–29).
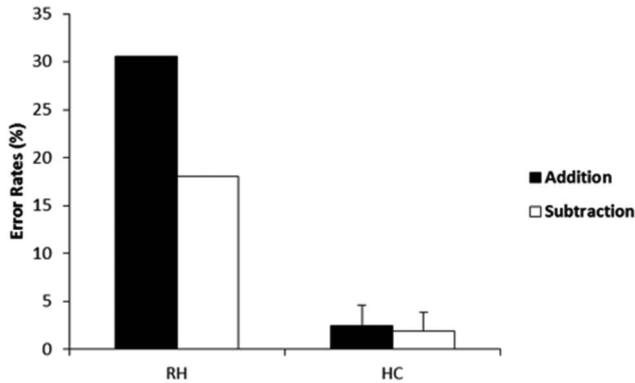
Figure 4. Error rates ($\pm SE$) in the arithmetic task for R.H. and HC as a function of operation (addition vs. subtraction).

Results. R.H. made more errors than HC (R.H.: 30/96; HC: 6.86 ± 6.41; $t(6) = 3.377$, $p = .015$), both in ascending (R.H.: 16/48; HC: 3.29 ± 3.49; $t(6) = 3.407$, $p = .014$) and descending order (R.H.: 14/48; HC: 3.57 ± 3.55; $t(6) = 2.748$, $p = .033$). We calculated the mean deviation from the midpoint for each interval length. A positive value indicates overestimation and a negative value indicates underestimation of the midpoint. R.H.'s mean deviation was 0.135, which was significantly different from the HC (-0.004 ± 0.135; $t(6) = 3.94$, $p = .008$). R.H.'s deviation was of 0.024 for the three-item intervals, 0.167 for the five-item intervals, 0.222 for the seven-item intervals, and 0.5 for the nine-item intervals (see Figure 5). This differed from the HC for the five-item intervals (HC: -0.024 ± 0.053; $t(6) = 3.337$, $p = .016$) and was marginally different for the seven-item intervals (HC: 0.032 ± 0.084; $t(6) = 2.124$, $p = .078$). No significant differences were observed for three-item intervals (HC: 0.01 ± 0.019; $t(6) = 0.68$, $p = .522$) or for nine-item intervals (HC:-0.12 ± 0.393; $t(6) = 1.473$; $p = .191$).

Discussion

A growing body of findings suggests that mental manipulation of numbers (e.g., Casarotti et al., 2007; Di Luca et al., 2013; Fischer et al., 2003) and solving arithmetic problems induces shifts of spatial attentional in healthy participants (e.g., Knops et al., 2009a; Masson & Pesenti, 2014; Mathieu et al., 2016; Werner & Raab, 2014; Yu et al., 2016). The present study was motivated by the scarcity of causal evidence demonstrating that attentional mechanisms play a central role in numerical processing and mental arithmetic and are not a mere byproduct of it. This study aimed to examine the performance of a right neglect patient in numerical tasks (number bisection, number comparison, mental arithmetic) that have been investigated only separately in studies with left neglect patients. If these tasks rely on similar attentional mechanisms, then it is expected that R.H. would show a deficit in processing numbers larger than the reference in numerical comparison tasks, a deficit for solving addition problems in mental arithmetic, and a deviation toward numbers smaller in numerical interval bisection.

In numerical comparison, R.H. showed selective RL increase when judging numbers just larger than the standards whereas his

performance was normal for smaller numbers. It is important to note that this pattern was found irrespective of the magnitude of the standard. For instance, processing digit 6 was slower than processing digit 4 when the standard was 5 whereas responding to digit 5 was faster than responding to digit 7 when the standard was 6. Because the number associated with increased RLs changes with the standard of comparison, R.H.'s difficulties are clearly not determined by the absolute magnitude of the presented numbers within the tested interval but rather by their relative magnitude compared with the specific standard. This interpretation implies that neglect does not affect representing the absolute magnitude of numbers per se but rather the process of shifting attention from one number to another on a magnitude scale. It is important to note that R.H.'s pattern of response is opposite to what was found in left neglect patients, who were slower in responding to numbers just smaller than the standard (e.g., Masson et al., 2013, 2016a; Salillas et al., 2009; Vuilleumier et al., 2004). Combined with the results of left neglect patients in past experiments, the results of this right neglect patient confirm that attentional shifts to the right or to the left are crucial for accessing the representation of a numerical magnitude located on the left or right relative to the standard.

In mental arithmetic, solving subtractions has been associated with leftward attentional shifts and solving additions to rightward shifts in healthy participants (Hartmann et al., 2016; Knops et al., 2009b; Marghetis et al., 2014; Masson & Pesenti, 2014; Mathieu et al., 2016; Werner & Raab, 2014). These compatibility effects could be viewed as epiphenomena that would not reflect a causal role of spatial attention for solving arithmetic problems. It has indeed been reported that operation signs could evoke by themselves spatial associations. This could mean that spatial attentional bias related to mental arithmetic would result from semantic associations between operator and space that do not play a part in the procedure that leads to solving the problem (Hartmann, Mast, & Fischer, 2015; Pinhas, Shaki, & Fischer, 2014). A recent study recording the eye movements of participants hearing additions or subtractions showed early upward gaze shifts when hearing plus signs and downward gaze shifts when hearing minus signs, hence before starting the procedure of calculation because the second operand was not yet known (Hartmann et al., 2015). Moreover, when participants were asked to classify plus and minus signs by
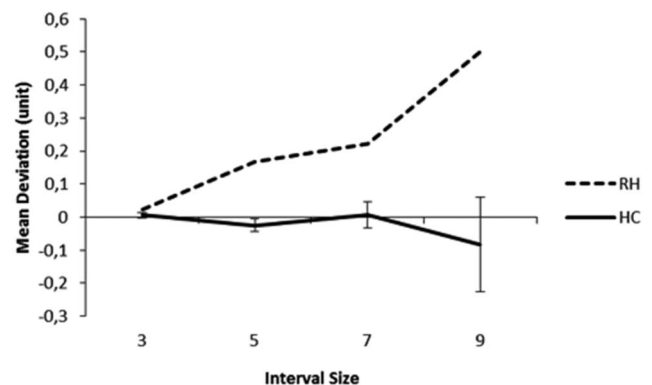

Figure 5. Mean deviation ($\pm SE$) from the midpoint (0) for R.H. and HC as a function of interval size. Positive and negative values indicate a deviation toward larger and smaller numbers, respectively.

pressing right and left response keys, responses were faster when the plus sign was associated with the right response key and the minus sign with the left response key (Pinhas et al., 2014). It is worth noting that this "operation sign spatial association" (OSSA) was only observed when the classification task was preceded by a task that made the mathematical context salient. To rule out that attentional shifts are merely byproducts of the solving procedures, we investigated the arithmetical performance of neglect patients that are impaired for orienting their attention to the contralesional side of space. A selective deficit in subtraction while solving addition problems was not affected was reported in left neglect patients (Dormal et al., 2014), suggesting a causal role of attentional mechanisms in mental arithmetic. In this study, we reported a case of a right representational neglect patient with a deficit in solving addition problems. Together with the previous study by Dormal and colleagues (2014), the present case provides a double dissociation between addition and subtraction performance that matches the orientation of neglect. This double dissociation has never been reported before and is hard to explain within the classical cognitive architectures of number processing and calculation. The solving of addition and subtraction problems, with a result or an operand larger than 10, requires calculation procedures such as decomposition and carrying or borrowing operations (Campbell & Xue, 2001; LeFevre, DeStefano, Penner-Wilger, & Daley, 2006; LeFevre, Sadesky, & Bisanz, 1996; Pesenti et al., 2001). It has also been proposed that calculation involves mental manipulation of number magnitude representations that were conceived as abstract (McCloskey, Caramazza, & Basili, 1985) or analogical taking the form of a spatial continuum in which numbers are aligned from left to right in increasing order (Dehaene, 1992). However, in these models, no distinction is made between the procedures and representations underlying the solving of large addition versus large subtraction problems.

This reverse pattern of impairment between left and right neglect constitutes strong evidence for the functional role of attention orientation in the procedures that take place when solving an arithmetic problem and demonstrates that attentional shifts in mental arithmetic are more than byproducts of the solving procedure. These results are in line with studies on healthy participants showing that hand movement direction (Wiemers, Bekkering, & Lindemann, 2014), eye movement direction (Masson, Pesenti, & Dormal, 2016b), or the location of the presentation of the second operand (Mathieu et al., 2016) could have an impact on mental arithmetic solving. Moreover, it has been reported that presenting flickering distractors on the left or right side of the screen impaired subtraction or addition solving in healthy participants (Masson & Pesenti, 2016). Critically, given that the magnitude of the results of addition and subtraction problems were equilibrated, the possibility that the pattern of arithmetic performance of R.H. is simply due to a deficit for processing large magnitudes can be excluded. As noted for number comparison, R.H.'s difficulties are not related to an impaired representation of number magnitude but to an impaired access to the numbers located rightward relative to the first operand of additions in right neglect patients or leftward relative to the first operand of subtractions in left neglect patients.

These findings lead us to propose that part of the procedure for solving an addition or a subtraction implies first representing a starting location (i.e., O1), and then, according to the operation, proceeding to an attentional shift toward the location of the re-

sponse that will be located on the left side for a subtraction and on the right side for an addition. Thus, right representational neglect that causes difficulty in orienting attention to the right side of mental space can also affect the ability to access the representation of the correct answer of an addition that is located on the right relative to the first operand, whatever the absolute magnitude of the response on a mental continuum. This mechanism would be recruited both when solving arithmetic problems and when performing numerical comparison by transiently mapping numbers onto a mental continuum centered on the standard of comparison. We conclude that attentional shifts may be functionally involved whenever one numerical magnitude has to be represented mentally relative to another. We would like to stress one aspect that is essential to keep our interpretation coherent with regard to the double dissociation principle: we argue that addition and subtraction rely on the same spatial-numerical representational medium but that distinct components are used to shift attention leftward and rightward along this medium. The double dissociation of subtraction or addition solving performance does not result from a globally impaired visuospatial representation of numbers or from a general impairment of attention orientation mechanisms but from a selective impairment of the mechanisms allowing respectively leftward or rightward attention shift to take place.

Considering numerical interval bisection, a deviation toward larger numbers in left neglect patients has long been considered as evidence for the existence of a spatial representation of number magnitude (Zorzi et al., 2002). This bias is mostly interpreted as reflecting an impaired representation of small numbers located on the left part of the continuum. Accordingly, right neglect patients were reported with a significant deviation toward smaller numbers (Pia et al., 2009; Woodbridge et al., 2013) and the severity of neglect was correlated to the deviation in numerical interval bisection (e.g., Pitteri et al., 2015; Yang et al., 2009). However, further studies have questioned the idea of a functional equivalence between the mental number line and physical space. Indeed, a double dissociation between numerical bisection and physical line bisection has been reported (Doricchi et al., 2005). This study found that only those patients presenting a prefrontal lesion, a region associated with working memory, showed a deviation toward larger numbers in numerical interval bisection and that these patients did not necessarily show neglect symptoms. Moreover, the size of the deviation in this task correlated with the impairment of spatial and verbal working memory (i.e., only participants with working memory impairment showed a deviation in numerical interval bisection). Thus, past studies investigating numerical interval bisection bias in neglect patients revealed ambiguous results and a recent group study suggests that the bias observed in numerical interval bisection could be related to multiple components or various strategies used by the participants aside from attentional or working memory deficits (Storer & Demeyere, 2014). Strikingly, in the present study, a right representational neglect patient shows a significant deviation toward larger numbers, which is exactly the same pattern as what was first observed in a group of left neglect patients (e.g., Zorzi et al., 2002). Our results corroborate the case study of another right neglect patient in which a similar deviation toward larger numbers was found in numerical interval bisection (van Dijck et al., 2011). Because their patient was selectively impaired in recognizing items at the start of memorized verbal sequences, these authors interpreted the rightward

deviation in numerical bisection displayed by their patient as a failure to maintain in working memory the first items of the ordinal sequence of numbers to be bisected. In bisection tasks, items at the beginning of the sequence were missed and the patient performed bisection on the remaining items, which provoked a deviation toward larger numbers. Likewise, R.H. was impaired for recognizing items at the beginning of the sequence, which might corroborate van Dijck et al.'s interpretation of numerical biases shown in the number bisection task. Although the working memory account of numerical interval bisection bias requires future investigation, the key point is that the orientation of neglect does not seem to determine the orientation of the numerical bias in numerical interval bisection for this patient. In numerical interval bisection, R.H. used mechanisms or strategies that seem distinct from those involved in number comparison and mental arithmetic. We suggest that the various strategies used by neglect patients to bisect numerical intervals are responsible for the diverging patterns of performance. If the strategy does not involve a spatial medium, then the deviation will not follow the direction of neglect.

One might suggest that the present case is atypical because brain lesions extend outside of the parietal areas that are usually related to neglect (e.g., Halligan et al., 2003; Vallar & Perani, 1986). However, several recent studies demonstrate that neglect can be the consequence of gray and/or white matter lesions in many different regions, inducing a disconnection of the spatial attention networks (e.g., Vuilleumier, 2013) and/or hypoactivity in one hemisphere (e.g., Corbetta & Shulman, 2011). In the present case, brain imaging data are limited to the investigation made for a clinical purpose and do not provide specific information about white matter damage apart from a possible mild demyelination in the left occipital and left anterior frontal white matter. Representational neglect is often associated with lesions in the right hemisphere (Bartoloméo, D'Erme, & Gainotti, 1994), but some studies have already reported cases exhibiting representational neglect after a left hemisphere lesion (Cocchini, Bartolo, & Nichelli, 2006; Pia et al., 2009; van Dijck, Gevers, Lafosse, & Fias, 2013). It has been suggested that representational neglect is difficult to evidence after a left hemisphere lesion, and is thus underdiagnosed, because most of the tests rely on the verbal system, the integrity of which is often compromised by the lesion (Salvato et al., 2014). The exact brain regions involved in the interaction between spatial attention and number manipulation, in neglect patients, remain to be identified. Brain imaging studies in healthy adults have shown increased activity in parietal and prefrontal regions during the generation and the manipulation of complex mental images (e.g., Kukolja et al., 2006; Sack, Camprodon, Pascual-Leone, & Goebel, 2005; Trojano et al., 2000). The use of voxel-based morphometry in a group of patients with and without neglect would help in specifying how these regions contribute to the asymmetric pattern of performance we observed in addition and subtraction tasks (see also Dormal et al., 2014). The distributed pattern of lesions shown by R.H. also raises the possibility that his impairment in numerical tasks is related to generalized temporal lobe pathology. However, at the time of the neuropsychological investigation, the subdural empyema extending in the temporal lobe had completely regressed and the patient did not show any clinical sign of aphasia. Although we cannot exclude subtle naming difficulties, these could not account for the asymmetrical performance in the addition and subtraction task because the two arithmetic operations were matched in terms of linguistic demands.

Finally, in R.H.'s case, right neglect extends to mental imagery, which might constitute the critical link between biases in numerical comparison, mental arithmetic, and attentional mechanisms. In some previous cases, a dissociation was found between perceptual and representational neglect (e.g., Beschin, Basso, & Della Sala, 2000; Guariglia, Padovani, Pantano, & Pizzamiglio, 1993), underlining the need to include representational neglect assessment when assessing the impact of neglect on numerical tasks. On the assumption that the reported difficulties in number comparison and mental arithmetic are a form of representational neglect extending to abstract cognitive abilities, the presence of numerical biases should be contingent on the presence of representational neglect as revealed by other tasks that proved to be sensitive to this dimension of spatial neglect such as clock-face tests (Grossi et al., 1989; Kukolja et al., 2006), geographic map descriptions (Rode et al., 1995), and cloud-like shapes tests (Bisiach et al., 1979; Ogden, 1985; van Dijck, et al., 2013).

Conclusion

Our systematic examination of the performance of a right neglect patient in numerical comparison and mental arithmetic indicates that spatial attention is recruited for localizing the relative position of a number or of the response of the problem. These results support the idea that neglect may extend to the manipulation of numbers on a representational medium, thus emphasizing the need to consider this dimension as part of the evaluation in future neuropsychological studies.

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