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Extra-powerful on the visuo-perceptual space, but variable on the number space:

Different effects of Optokinetic stimulation in neglect patients

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ABSTRACT

We studied the effects of optokinetic stimulation (OKS; leftward, rightward, control) on the visuo-perceptual and the number space, in the same sample, during line bisection and mental number interval bisection tasks. To this aim we tested six patients with right-hemisphere damage and neglect, six patients with right-hemisphere damage but without neglect, and six neurologically healthy participants. In patients with neglect, we found a strong effect of leftward OKS on line bisection, but not on mental number interval bisection. We suggest that OKS influences the number space only under specific conditions.

Keywords: neglect, optokinetic stimulation, visual line bisection, mental number line, number space, spatial attention orienting, visuo-motor processing

Word count (main text): 5135 words

1. INTRODUCTION

There is considerable evidence from behavioral, neuropsychological, and neuroimaging studies on the existence of a close relation between numbers and space (for reviews see, de Hevia, Vallar, & Girelli, 2008; Fias & Fischer, 2005; Umiltà, Priftis, & Zorzi, 2009). The interaction between numbers and space suggests that numerical representation might be deeply rooted in cortical networks that also subserve spatial cognition (for review see, Hubbard, Piazza, Pinel, & Dehaene, 2005). One of the most widely replicated effects that imply the presence of an interaction between numbers and space is the *Spatial Numerical Association of Response Codes* (SNARC) effect. When participants are asked to judge whether a number is odd or even, by pressing a left-sided or right-sided button, reaction times (RTs) are faster when participants respond to relatively larger numbers (e.g., 9) with the right-sided button than with the left-sided button, whereas the opposite is observed for relatively smaller numbers (e.g., 1; Dehaene, Bossini, & Giraux, 1993). Interestingly, this effect was also obtained by crossing the participants' hands, suggesting its strict relation with space-based coordinates, rather than with effector-based coordinates (Dehaene et al., 1993). The interpretation of the SNARC has been grounded on number magnitude representation in the form of a mental number line (MNL), which is spatially oriented from left-to-right –at least in left-to-right reading cultures– with relative smaller numbers on the left and relative larger numbers on the right (but see, Gevers, Verguts, Reynvoet, Caessens, & Fias, 2006).

Strong evidence supporting the MNL hypothesis comes from neuropsychological studies on patients with left neglect (LN). LN patients, following right-hemisphere lesions, fail to report, orient to, or verbally describe stimuli in the contralesional side of space (i.e., the left side; for review see, Halligan, Fink, Marshall, & Vallar, 2003). When LN patients

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are asked to bisect visual line segments, they systematically show a bias to the right of the true midpoint of the visual segment, as if they were ignoring its leftmost part. Halligan and Marshall (1988; Marshall & Halligan, 1989) observed that this rightward bias is directly proportional to the length of the visual segments. That is, the longer the segment, the greater the bias to the right of its true midpoint, although a leftward bias was observed for the shortest segments (i.e., the crossover effect).

To investigate whether the MNL has spatial features similar to those of visual line segments, Zorzi, Priftis, and Umiltà (2002) asked right-hemisphere-damaged patients with LN to mentally bisect numerical intervals (e.g.,"Which is the number lying halfway between 1 and 9?"). The results showed that LN patients bisected to the right of the true midpoint of longer number intervals (e.g., responding that "7" is halfway between "1" and "9"), but they misbisected to the left of the true midpoint for shorter number intervals (e.g., responding that "6" is halfway between "7" and "9"). Thus, the overall pattern observed in the mental number interval bisection resembled that of LN patients during the bisection of visual segments. The performance of LN patients on number interval bisection led Zorzi et al. to propose a functional isomorphism between the number space and the visuo-perceptual space. Note, however, that our definition of functional isomorphism is somewhat different from that of Putnam (1975). According to our definition, functional isomorphism between a visual line and the mental number line means that:

1. Any point along a visual line or along the mental number line can be defined by using the same metrics (e.g., the x-axis on Cartesian axes). That is, by using the x-axis and an abstract point of reference indicating the origin of the x-axis (i.e., 0), positions to the left (x-) or to the right (x+) of this origin can be defined both on the mental number line and on a visual line.

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2. Two contiguous numbers on the mental number line can be represented as two contiguous points on a visual line.

3. Shorter/longer intervals between two numbers (e.g., 1-3, 1-9) can be represented by shorter/longer segments on a visual line.

All these principles regarding what we have termed a "functional isomorphism" between the number space (i.e., MNL) and the perceived space have received special interest in the centuries, for practical reasons. For instance, the use of rulers exemplify how the number space can be mapped on a visual line by applying the principles of a functional isomorphism.

The findings of Zorzi et al. (2002) have been replicated and extended in a number of recent studies reporting that LN patients show spatial biases in number processing tasks (Cappelletti, Freeman, & Cipolotti, 2007; Hoeckner et al., 2008; Klein et al., 2013; Loftus, Nicholls, Mattingley, & Bradshaw, 2008; Priftis, Zorzi, Meneghello, Marenzi, & Umiltà, 2006; Priftis et al., 2008; Priftis, Pitteri, Meneghello, Umiltà, & Zorzi, 2012; Rossetti et al., 2004; Salillas, Granà, Juncadella, Rico, & Semenza, 2009; Vuilleumier, Ortigue, & Brugger, 2004; Yang, Tian, & Wang, 2009; Zamarian, Egger, & Delazer, 2007; Zorzi, Priftis, Meneghello, Marenzi, & Umiltà, 2006; for review see, Umiltà et al., 2009).

The effects of LN on the number space, however, might also be explained by recent theories that dispense with the spatial coding of numbers (e.g., see Rossetti et al., 2011; Van Dijck & Fias, 2001). For instance, Van Dijck, Gevers, Lafosse, Doricchi, and Fias (2011; see also Van Dijck, & Fias, 2011) have suggested that the effective position-based coding of stimuli in verbal working memory might be crucial for numerical tasks that are usually thought to involve purely spatial representations of numerical magnitudes. The working memory hypothesis, however, cannot explain effects of LN on the number space

on tasks that require minimal or similar working memory resources (Priftis et al., 2008; Salillas, Granà, Juncadella, Rico, & Semenza, 2009; Vuilleumier, Ortigue, & Brugger, 2004; Zorzi, Priftis, Meneghello, Marenzi, & Umiltà, 2006; for review see, Umiltà et al., 2009). Another hypothesis has been recently advanced by Aiello et al. (2012) and Aiello, Merola, & Doricchi (2012), who have suggested that right-hemisphere-damaged patients (with or without LN) have deficits in processing small numbers (1-9). Nonetheless, this hypothesis cannot explain why effects of LN for the number space are, in many studies, selectively present only in right-hemisphere-damaged patients with LN (for review see, Umiltà et al., 2009) and why these effects are present even when larger numbers (> 9) have been employed (Hoeckner et al., 2008; Klein et al., 2013; see also Goebel et al., 2006, for evidence from a TMS study on healthy participants).

Numerous studies have demonstrated that sensory stimulations can reduce several visuo-spatial deficits of LN patients. For instance, vestibular caloric stimulation (Rubens, 1985; Vallar, Sterzi, Bottini, & Rusconi, 1990), neck muscle vibration (Karnath, Christ, & Hattie, 1993), transcranial magnetic stimulation (Oliveri et al., 2001), transcranial direct current stimulation (Ko, Han, Park, Seo, & Kim, 2008), and optokinetic stimulation (Mattingley, Bradshaw, & Bradshaw, 1994; Pizzamiglio, Frasca, Guariglia, Incoccia, & Antonucci, 1990) have been reported to be effective in reducing visuo-spatial deficits of LN patients. Among these, a simple, non-invasive visual stimulation technique used to treat visuo-spatial deficits of LN patients is the optokinetic stimulation (OKS). OKS consists of multiple dots –or vertical stripes– moving coherently along the horizontal plane (i.e., leftwards or rightwards), inducing the optokinetic nystagmus (OKN) in absence of a fixation point. OKN is a characteristic eye movement composed by a slow phase towards the direction of the OKS (i.e., pursuit eye movement), followed by a rapid phase opposite

to the OKS direction (i.e., saccadic eye movement). OKS has been reported to improve several visuo-spatial aspects of LN patients, such as the visual line bisection error (Mattingley et al., 1994; Pizzamiglio et al., 1990), the ipsilesional deviation of the subjective visual straight ahead (Karnath, 1996), the visual size distortion and the distance coding (Kerkhoff, 2000; Kerkhoff, Schindler, Keller, & Marquardt, 1999), neglect dyslexia (Reinhart, Schindler, & Kerkhoff, 2011), and the position sense (Vallar, Antonucci, Guariglia, & Pizzamiglio, 1993; Vallar, Guariglia, Magnotti, & Pizzamiglio, 1995). OKS has been also shown to be effective in reducing –even if temporarily– sensory and motor defects (Vallar, Guariglia, Nico, & Pizzamiglio, 1997), and auditory neglect (Kerkhoff et al., 2012). Moreover, sessions of repetitive leftward OKS (rL-OKS) have been reported to induce long-lasting effects up to two weeks after OKS treatment in cancellation tasks, visuo-perceptual line bisection, visuo-manual line bisection, size distortion, and omissions in text reading (Kerkhoff, Keller, Ritter, & Marquardt, 2006). Many of these studies (Karnath, 1996; Pizzamiglio et al., 1990; Vallar et al., 1993, 1995) have shown that rightward OKS has negative effects in LN patients, with a decline in performance compared to static OKS or in the absence of any stimulation, In some of these studies, however, the negative effects of rightward OKS have not been confirmed (e.g., Vallar et al., 1993).

Because of the association between the numerical space and the visuo-perceptual space, similar effects on numerical and visuo-perceptual tasks have been found, through the use of techniques that require visuo-spatial adaptation. Rossetti et al. (2004), indeed, first reported effects of visuo-motor stimulation on mental number representation. Through the exposure to prismatic-goggles shifting the visual field 10 degrees to the right, Rossetti et al. showed that two LN patients improved in bisecting mental number intervals. This

finding has been taken as evidence of the effects of visuo-motor adaptation on the number space. On the same theoretical account, there are two other studies that have reported effects of visuo-perceptual stimulation on mental number representation. In the first one, Salillas et al. (2009) used random dot kinetograms (RDKs, i.e., a large number of moving dots randomly positioned within a restricted area on a PC screen) to influence the number space. The Authors tested a group of LN patients (RHDN+), a group of age-matched, right-hemisphere-damaged patients without LN (RHDN-), and an age-matched group of neurologically healthy participants (NHP), in a number comparison task (i.e., "Is the presented number smaller or larger than the reference number 5?"). The task was carried out during leftward, rightward, or random RDKs. Participants had to fix their gaze on a central fixation point during the experiment, so that the single pattern of dot displacement could not be tracked and, thus, the OKN could not be elicited. In the random RDKs condition and in the rightward RDKs condition, RHDN+ patients were slower in processing the number to the left of the reference one (i.e., 4), than in processing the number to the right of the reference one (i.e., 6; see also, Vuilleumier et al., 2004; Zorzi et al., 2012). Leftward RDKs, however, reduced the difference in processing numbers 4 and 6. In contrast, the RDKs effect was not present in RHDN- patients or in NHP. The results of Salillas et al. suggest that covert orienting of spatial attention, induced by the perception of leftward RDKs towards the contralesional visuo-perceptual space, can temporarily restore the impaired access to the MNL in LN patients.

In the second study, Priftis et al. (2012) reported the effect of OKS on number representation, by testing one LN patient (BG) and four RHDN- patients by means of the mental number bisection task (i.e., "What is the number lying halfway between 1 and 9?"). All patients were tested under static, leftward, and rightward OKS conditions. In the static

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and rightward OKS conditions, BG bisected towards larger numbers, whereas BG's performance dramatically improved following leftward OKS condition. These findings again support the notion that OKS can influence the number space representation. It should be noted, however, that in contrast to Salillas et al. (2009), Priftis et al. used optokinetic stimuli constituted by vertical black-and-white stripes instead of RDKs. Moreover, there was no fixation point and the participants were allowed to track the optokinetic stimuli so that OKN could be elicited. The findings of Priftis et al. suggest that even a different form of optokinetic stimulation (i.e., vertical black and white stripes) and the presence of OKN can temporarily restore the impaired access to the MNL in LN patients.

Both the findings by Salillas et al. (2009) and Priftis et al. (2012) are well explained by the theoretical account of the functional isomorphism between the visuo-perceptual space and the number space, as originally proposed by Zorzi et al. (2002). Indeed, the two spaces seem to have similar metrics and can be modulated by the organization of similar, although independent, spatial attention mechanisms (see also Zorzi et al., 2012). Nevertheless, several Authors have found that the rightward bias observed in the mental number bisection task in right-hemisphere-damaged patients is not correlated with the severity or the presence of an analogous bias in visuo-perceptual space (Doricchi et al., 2005, 2009; Loetscher et al., 2010; Loetscher & Brugger, 2009; Pia et al., 2012; Rossetti et al., 2004; van Dijck et al., 2011a,b; for review see, Rossetti et al., 2011). Note, however, that the notion of the functional isomorphism between the visuo-perceptual space and the number space implies that the MNL and the visual lines have *similar* (not identical) spatial properties. This notion does not require any common representation or shared neural mechanisms (Zorzi et al., 2012) and implies that dissociations between the number space and other spaces (e.g., visuo-perceptual) can occur, as systematically reported both in

group and single case studies (Aiello et al., 2012a,b; Doricchi et al., 2005, 2009; Loetscher & Brugger, 2009; Loetscher, Nicholls, Towse, Bradshaw, & Brugger, 2010; Pia et al., 2012; Rossetti et al., 2004, 2011; Tian Yet et al., 2011; van Dijck et al., 2011a,b Zorzi et al. 2004). Despite the presence of dissociations, however, several studies have also reported different forms of association between the number space and the visuo-perceptual space on neurologically healthy participants. These findings are in favor of attention-mediated interactions between the visuo-perceptual space and the number space. For instance, the involvement of visuo-spatial attention in number processing is clearly supported by the findings that numerical cues can orient spatial attention in the visuo-perceptual space (Bonato, Priftis, Marenzi, & Zorzi, 2008; Casarotti, Michielin, Zorzi, & Umiltà, 2007; Cattaneo, Silvanto, Battelli, & Pascual-Leone, 2009; Fischer, Castel, Dodd, & Pratt, 2003). Even more important is the demonstration of the interaction in the opposite direction (i.e., with visuo-spatial processing influencing number processing), thereby showing that the spatial aspects of numerical processing are not epiphenomenal (Zorzi et al., 2012). For instance, Stoianov, Kramer, Umiltà, and Zorzi, (2008; see also Kramer, Stoianov, Umiltà, & Zorzi, 2011) found that an irrelevant visuo-spatial cue can prime a target number in both magnitude comparison and parity judgments requiring vocal, non-spatial responses. Moreover, Nicholls and McIlroy (2010) found similar effects on a number interval bisection task.

To summarize, previous studies have shown a strict connection between the number space and the visuo-perceptual space (for review see, Umiltà et al., 2009). With respect to visuo-perceptual stimulations, it has been shown that leftward OKS can improve the processing of the visuo-perceptual space (Mattingley et al., 1994; Pizzamiglio et al., 1990) and the processing of the number space (Priftis et al., 2012; Salillas et al., 2009) in LN

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patients, in a similar way. Until now, however, there are no studies that have directly compared OKS effects both on visual line bisection and on mental number interval bisection in the same sample. We aimed to investigate whether OKS could affect the visuo-perceptual and the number space, by directly comparing LN patients' performance on visual line bisection and on mental number interval bisection. We expected to find similar patterns of performance of LN patients on both tasks, by using the same type of OKS. Specifically, during leftward OKS, we expected better performance of LN patients in both visual line bisection and mental number interval bisection. In contrast, we expected no significant effects of rightward OKS compared to the two control conditions (i.e., static and mixed OKS conditions – see the Methods for details). Finally, we expected no effects of OKS conditions (leftward and rightward) in control participants (i.e., RHDN+ and NHP).

2. GENERAL METHOD

2.1. Participants

Six RHDN+ following right-hemisphere stroke (mean age = 61.1 years, SD = 10.2; mean education = 6.3 years, SD = 2.3), six RHDN- following right hemisphere stroke (mean age = 54.1 years, SD = 11.9; mean education = 11.8 years, SD = 2.2), and six NHP (mean age = 61.9 years, SD = 14; mean education = 12.7 years, SD = 3.3) took part in the present study, after giving their informed consent according to the Declaration of Helsinki II. Demographic, clinical, and psychometric data of the participants are reported in Table 1. Time since lesion was not significantly different between RHDN+ and RHDN-, $t(10)$ = .923, ns. Age was not significantly different among groups, $F(2, 15)$ = .757, ns.

[TABLE 1]

Inclusion criteria for all participants comprised absence of dementia, substance abuse, and psychiatric disorders. All patients had unilateral right-hemisphere lesions after ischaemic or hemorragic stroke, documented by Computerized Axial Tomography (CAT) or Magnetic Resonance Imaging (MRI) scans. LN was assessed through a standardized neglect battery (conventional tests of the Behavioral Inattention Test, BIT; Wilson, Cockburn, & Halligan, 1987). Patients were further assessed through the digit span test (from the WAIS-R; Wechsler, 1997) to assess short-term memory (forward presentation) and working memory (backward presentation), and the main subtests of the Number Processing and Calculation battery (NPC; Delazer, Girelli, Granà, & Domahs, 2003) to assess general numerical abilities. RHDN+ and RHDN- patients had good short-term memory, working memory, and numerical abilities (see Table 2). Each patient had normal or corrected-to-normal visual acuity. All patients responded to OKS by showing a normal OKN.

[TABLE 2]

2.2. Apparatus and stimuli

Optokinetic stimuli were composed by 200 yellow dots (diameter = 11.33 pixels) presented against a black background of a laptop PC screen (14.1 inches TFT display with a resolution of 1440 x 900 pixels). The laptop PC was powered by a 2 GHz CPU with 3 GB SDRAM. The dots were presented in four different conditions: static (i.e., static dots), mixed (i.e., composed of dots moving leftwards, rightwards, upwards, or downwards),

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leftward (i.e., moving dots towards the left), and rightward OKS (i.e., moving dots towards the right). The speed of the dots was 8.5°/s. The static and the mixed conditions were considered as control conditions.

2.3. General procedure

Each experiment (Experiment 1: visual line bisection; Experiment 2: mental number interval bisection) encompassed a preliminary session, followed by the experimental session. In the preliminary session, participants sat in front of the laptop PC screen. A chinrest was used to keep the eyes of the participants at a constant distance of 40 cm from the laptop PC screen. Participants were asked to fix their gaze on the center of the laptop PC screen, while either leftward and rightward OKS was presented, one at a time, to check for the presence of normal OKN. All participants had normal OKN, characterized by a slow phase of eye movement towards the direction of the OKS and a rapid phase opposite the direction of the OKS. In the experimental session, participants were positioned in front of the laptop PC screen, with their head fixed in the chinrest. Participants were asked to fix their gaze on the center of the laptop PC screen. OKS was presented to the participants in four separate blocks (static, mixed, leftward, rightward), in four consecutive days (one block each day) to avoid after-effects of the OKS stimulation stream. The order of OKS conditions, and the order of Experiments 1 and 2 were counterbalanced within and across participants.

3. EXPERIMENT 1: VISUAL LINE BISECTION

3.1. METHODS

3.1.1. Stimuli

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Twenty light-red-colored line segments (length: 25, 100, 175, 250 mm) were presented at the center of a laptop PC screen, one segment at a time. The height of each line segment was 1 cm. Each line segment length was presented five times. The presentation sequence of the line segments was randomized, but it was the same for all participants and in all OKS conditions.

3.1.2. Procedure

We presented OKS, by using a dedicated software (*VS,* www.medical-computing.de; Kerkhoff & Marquardt, 2009). The experiment was run in a quiet, dimly-light room without visual distractors or acoustic noise. The participants were seated in front of the laptop PC screen, in a comfortable position. The laptop PC screen was aligned with the midline of each participant's body trunk. By means of a chinrest, the eyes were kept at a constant distance of 40 cm from the laptop PC screen. Participants were presented with single line segments displayed on the laptop PC screen. The experimenter was seated behind each participant, and moved a thin, vertical black segment by clicking the button of a wire-less mouse. The vertical segment could start moving from the left or from the right side of the line segment in separated, counterbalanced blocks. Participants were required to say: "Stop!" when they thought that the vertical segment, moved by the experimenter, was approximately on the center of the line segment.

3.1.3. Design

A mixed design was used. The within participants factors were: OKS condition (four levels: static, mixed, leftward, rightward), Line length (four levels: 25, 100, 175, 250 mm), and Starting-point (two levels: left, right). The between participants factor was Group

(three levels: RHDN+, RHDN-, NHP). The dependent variable was the mean difference (d) between observed (O) and correct (C) responses (i.e., dO-C). Positive values correspond to a rightward deviation with respect to the center of each line segment and negative values correspond to a leftward deviation with respect to the center of each line segment.

3.2. RESULTS

The dO-C was calculated for each participant and for each line segment. For each condition considered (i.e., OKS, Starting-point, Line length), responses above or below 2 *SD* from the mean were excluded from the statistical analyses (trimmed outliers < 1%). Then, for each participant, OKS, and Starting-point a regression analysis was conducted with Line length as the predictor and mean dO-C as the outcome. The resulting betas were entered in a three-way mixed analysis of variance (ANOVA) with Group (RHDN+, RHDN-, NHP) as the between participants factor, and with OKS condition (static, mixed, leftward, rightward) and Starting-point (left, right) as within participants factors.

The results of the mixed ANOVA revealed a main effect of OKS, $F(2.787, 41.801) = 5.37$, $p < .01$, partial eta squared = .264. Post-hoc comparisons (corrected with Bonferroni) revealed that the leftward OKS condition (mean betas = -0.001) differed from the static OKS condition (mean betas = 0.032), $p < .05$. All other comparisons were not significant. The main effect of Starting-point was significant (mean betas starting from the left endpoint = 0.004, mean betas starting from the right endpoint = 0.033), $F(1, 15) = 7.41$, $p < .05$, partial eta squared = .331. The double interaction between OKS and Group was significant, $F(5.573, 41.801) = 6.696$, $p < .001$, partial eta squared = .472. Post-hoc comparisons (corrected with Bonferroni) were conducted for each group. For the RHDN+

group, leftward OKS induced a progressive leftward bisection shift as a function of line length (mean betas = -0.033), which was significantly different from all the rightward bisection bias observed following static (mean betas = 0.061), mixed (mean betas = 0.045), and rightward OKS (mean betas = 0.058); all ps < .05 (see Figure 1a). The differences among the rightward shifts in the static, mixed, and rightward OKS conditions were not significant. For the RHDN- and the NHP, all paired comparisons were not significant (see Figures 1b and 1c). All other main effects and interactions were not significant.

[FIGURES 1a, b, c]

4. EXPERIMENT 2: MENTAL NUMBER INTERVAL BISECTION

4.1. METHODS

4.1.1. Stimuli

Stimuli consisted of number pairs with a length of three (e.g., 1-3), five (e.g., 1-5), seven (e.g., 1-7), or nine (e.g., 1-9). The same number intervals were repeated within the units (i.e., single digits from 1 to 9; e.g., 1-7), the teens (i.e., numbers from 11 to 19; e.g., 11-17), and the twenties (i.e., numbers from 21 to 29; e.g., 21-27). The final set of stimuli comprised 48 number pairs subdivided into 16 pairs within the units, 16 pairs within the teens, and 16 pairs within the twenties. The presentation sequence of the number pairs was randomized, but it was the same for all participants and in all OKS conditions.

4.1.2. Procedure

OKS was presented using a dedicated software (*VS,* www.medical-computing.de; Kerkhoff & Marquardt, 2009). The experimenter sat behind a laptop PC screen, out of the

participants' view. By using a camcorder, the experimenter controlled whether the participants directed their gaze on the center of the laptop PC screen. Following oral presentation of each number pair, participants were asked to orally report the number lying halfway between the first and the second number of each pair (e.g., Experimenter: "Which number is halfway between 1 and 9?"). For each participant, the 48 number pairs were presented twice (i.e., 96 trials). The whole task was then consequently administered in the backward presentation to counterbalance order effects (e.g., Experimenter: "Which number is halfway between 9 and 1?"). Thus, for ach participant the total number of trials was 192 (forward and backward presentation). There was no time limit for responding, but participants were required to give their answer as soon as possible, without performing calculation.

4.1.3. Design

A mixed design was used. The within participants factors were: OKS condition (four levels: static, mixed, leftward, rightward), Number interval length (four levels: 3, 5, 7, 9), and Presentation (forward, backward). The between participants factor was Group (three levels: RHDN+, RHDN-, NHP). The dependent variable was the mean arithmetic difference (d) between the observed (O) and the correct (C) responses in the mental number bisection task (i.e., dO-C).

4.2. RESULTS

The dO-C was calculated for each participant and for each number interval length. For each participant and condition (i.e., OKS, Presentation, Number interval length), responses above or below 2 SD from the mean were excluded from the statistical analyses (trimmed

outliers < 4%). A regression analysis was conducted for each participant, OKS, and presentation with the number interval length as the predictor and the mean dO-C as the outcome. On the static OKS condition, an one-sample t-test showed that the betas of RHDN+ were significantly different from 0, $t(5) = 4.085$, $p < .001$, whereas the betas of RHDN- were not, $t(5) = 1.937$, ns.

Betas were entered into a three-way mixed ANOVA with Group (RHDN+, RHDN-, NHP) as the between participants factor, and with OKS condition (static, mixed, leftward, rightward) and Presentation (forward, backward) as the within participants factors. The main effect of presentation was significant (mean betas of forward presentation = 0.155, mean betas of backward presentation = -0.011), $F(1, 15) = 13.509$, $p < .01$, partial eta squared = .474. All other main effects and interactions were not significant. In contrast with the verbal working memory hypothesis (Van Dijck & Fias, 2011), there was no correlation between digit spans and betas on number interval bisections in the static OKS condition (Digit span forward-betas, $rho = .018$, $p = .957$; Digit span backward-betas, $rho = -0.313$, $p = .321$).

[FIGURE 2]

5. DISCUSSION

Previous studies have suggested that OKS can ameliorate processing both of the visuo-perceptual space (Karnath et al., 1996; Kerkhoff, 2000, 2003; Kerkhoff et al., 1999, 2006, in press; Mattingley et al., 1994; Pizzamiglio et al., 1990; Vallar et al., 1993, 1995) and of the number space (Priftis et al., 2012; Salillas et al., 2009). These findings are in favour of a functional isomorphism between the visuo-perceptual space and the number space. There

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are several evidences, indeed, that the two spaces seem to have similar metrics and can be modulated by the organization of similar, though independent spatial attention mechanisms (Cappelletti et al., 2007; Hoeckner et al., 2008; Loftus et al., 2008; Priftis et al., 2006, 2008, 2012; Rossetti et al., 2004; Vuilleumier et al., 2004; Yang et al., 2009; Zamarian et al., 2007; Zorzi et al., 2006, 2012; for review see, Umiltà et al., 2009).

In the present study we tested the effects of OKS on the visual line bisection and on the mental number interval bisection tasks, in order to directly compare, for the first time and in the same sample, the role of OKS in spatial attention orienting in the visuo-perceptual space and in the number space. In Experiment 1 (visual line bisection task) we replicated the results of studies that had shown the effects of leftward OKS on the visuo-perceptual space (Mattingley et al., 1994; Pizzamiglio et al., 1990). Furthermore, in the present study OKS haseven inverted the rightward bias of LN patients: that is, the longer the segment, the greater the bias to the *left* of its true midpoint, resembling a sort of transient "opposite neglect" (i.e., right neglect). On the contrary, we found no significant OKS effect on control groups (i.e., RHDN- and NHP).

In Experiment 2 (mental number interval bisection), our results did not show any effects of OKS on the number space. We expected to find a restorative effect of leftward OKS in LN patients on the number interval bisection task, as reported in previous studies (Priftis et al., 2012; Salillas et al., 2009). Experiment 2 failed to replicate the results previously described in the literature, raising some theoretical speculations principally based on methodological differences among the studies. For instance, Salillas et al. (2009) presented a yellow cross in the center of the PC screen for the entire duration of the numerical task, except when the number to be compared substituted the fixation cross. Thus, in all trials both the yellow cross and the digit visually presented on the PC screen

functioned as a fixation point that did not allow the OKN. Thus, leftward RDKs temporarily restored the number space in LN patients probably because of a mechanism of covert spatial attention orienting, similar to that reported for visual lines both in the present and in the previous studies (Mattingley et al., 1994; Pizzamiglio et al., 1990). In the line bisection task, indeed, the horizontal line segment works like a fixation point, avoiding the OKN.

Nevertheless, if participants are allowed to track the OKS's motion in the absence of a fixation point, OKN is elicited. With the presence of OKN, Priftis et al. (2012) found restorative effects of leftward OKS on the number space in a LN patient. This observation suggests that also in the absence of a fixation point, leftward OKS can affect the number space through a mechanism of overt spatial attention orienting (Posner, 1980; for review see, Wright & Ward, 2008), in which the focus of spatial attention is directed towards the contralesional side of the visuo-perceptual space. The shift of visuo-spatial attention in the visuo-perceptual space may cue the contralesional side of the number space and, as a result, similar effects can be detected. This explanation, however, seems to be in contrast with the findings of previous studies showing that OKS induces covert shifts of spatial attention towards the side *opposite* that of the OKS direction (i.e., the *in-coming* side; Bense et al., 2006; Teramoto, Watanabe, Umemura, Matsuoka, & Kita, 2004) or a facilitation of responses in the *in-coming* side of OKS on a Simon task (Figliozzi, Silvetti, Rubichi, & Doricchi, 2010) in neurologically healthy participants. Nonetheless, LN patients are affected by cerebral lesions and their eye movements could be quite different in exploring the visuo-perceptual space (Behrmann, Watt, Black, & Barton, 1997; Karnath, Neiemeier, & Dichgans, 1998).

With respect to the present study, Priftis et al. (2012) used a type of OKS (i.e., vertical black-and-white stripes instead of dots) that has been more efficient to elicit overt spatial attention orienting mechanisms, which, in turn, were able to influence the number space. As originally proposed by Priftis et al. (2008), the preference for larger numbers observed in LN patients could be an instance of the ipsilesional hyper-attention and/or contralesional hypo-attention that, in the visuo-perceptual space as in the number space, manifests itself as a disengage deficit. That is, LN patients would have difficulties to disengage their spatial attention from larger magnitudes placed on the right of the MNL. Thus, only a strongly lateralized visual stimulation (leftward for LN patients) has the power to orient visuo-spatial attention towards the contralesional side of the affected number space.

An alternative account for the selective effects of OKS on the visuo-perceptual space, can be that of the double dissociation (Doricchi et al., 2005, 2009; Loetscher et al., 2010; Loetscher & Brugger, 2009; Pia et al., 2012; Rossetti et al., 2004; van Dijck et al., 2011a,b; for review see, Rossetti et al., 2011) reported between the processing of the two spaces (i.e., number vs. visuo-perceptual). That is, OKS influences only the processing of the visuoperceptual space, but not that of the number space, given that the two spaces have distinct spatial properties. If this were the case, however, one cannot explain why in the studies by Salillas et al. 2009 and Priftis et al. 2012, different types of OKS had, indeed, an effect on the processing of the number space (see also the "Introduction" for different instances of bilateral interaction between the number and the visuoperceptual space).

We rather suggest that OKS might influence the number space, but only under specific conditions. Indeed, the functional isomorphism between the number and the visuo-perceptual space does not mean that the two spaces are supported by a common

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representation. The two spaces, instead, are implemented in the brain through distinct

representations, which can interact under certain conditions.

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TABLES

TABLE 1

Participant	Gender	Age (years)	Education (years)	Onset of illness (months)	Handedness	Lesion site	Left visual field defects
RHDN+_1	M	63.1	8	1	R	MCA-R	-
RHDN+_2	M	53.1	9	3.3	R	MCA-R	+
RHDN+_3	M	78.4	5	3.1	R	MCA-R	+
RHDN+_4	F	52	8	19.4	R	CN-R	+
RHDN+_5	F	65.7	5	7.4	R	FTP-R	-
RHDN+_6	M	54.1	3	1.9	R	FTP-R	-
	Mean	**61.1**	**6.3**	**6**			
	(SD)	**(10.2)**	**(2.3)**	**(6.9)**			
RHDN-_1	F	65.7	12	1.4	L	MCA-R	-
RHDN-_2	M	45.7	12	3.9	R	MCA-R	-
RHDN-_3	M	41.7	11	3.6	R	MCA-R	+
RHDN-_4	F	70.1	10	2.4	R	MCA-R	-
RHDN-_5	F	56.6	10	3.6	R	MCA-R	+
RHDN-_6	M	44.7	16	238	R	MCA-R	-
	Mean	**54.1**	**11.8**	**42.2**			
	(SD)	**(11.9)**	**(2.2)**	**(96)**			
NHP_1	M	79.1	12	-	R	-	-
NHP_2	M	56.1	12	-	R	-	-
NHP_3	M	74.6	10	-	R	-	-
NHP_4	F	48.4	13	-	L	-	-
NHP_5	M	45.4	19	-	R	-	-
NHP_6	F	68	10	-	R	-	-
	Mean	**61.9**	**12.7**				
	(SD)	**(14.0)**	**(3.3)**				

Demographic, clinical, and psychometric data of the participants. MCA-R = middle cerebral artery-right; CN-R = capsular nucleus-right; FTP-R = frontal-temporal-parietal-right.

TABLE 2

Patient	[1]BIT Conv.	[2]Digit span	[3]Verbal counting	[3]Parity judgment (verbal)	[3]Number comparison (verbal)	[3]Addition facts (verbal)	[3]Subtraction facts (verbal)	[3]Reading arabic numerals
RHDN+_1	117*	4+3	0/2*	6/10*	9/10*	20/20	14/18*	17/18*
RHDN+_2	76*	6+3	2/2	10/10	10/10	20/20	18/18	11/18*
RHDN+_3	108*	5+3	2/2	10/10	10/10	20/20	18/18	6/18*
RHDN+_4	122*	5+3	2/2	10/10	10/10	18/20	16/18	18/18
RHDN+_5	115*	7+4	2/2	10/10	10/10	20/20	18/18	18/18
RHDN+_6	122*	6+4	2/2	10/10	10/10	20/20	18/18	18/18
RHDN-_1	140	7+5	2/2	10/10	10/10	20/20	18/18	18/18
RHDN-_2	134	6+4	2/2	7/10*	10/10	20/20	18/18	18/18
RHDN-_3	137	6+4	2/2	10/10	10/10	20/20	18/18	17/18*
RHDN-_4	138	6+3	2/2	10/10	10/10	20/20	18/18	18/18
RHDN-_5	139	6+4	2/2	9/10*	10/10	20/20	18/18	18/18
RHDN-_6	143	6+6	2/2	10/10	10/10	20/20	18/18	18/18

[1] Wilson, Cockburn, and Halligan (1987)

[2] Wechsler (1997)

[3] Delazer, Girelli, Granà, & Domahs (2003)

Patients' performance (RHDN+ and RHDN-) on neuropsychological tests. Scores below the cut-off are marked with an asterisk (*).

FIGURE LEGENDS

FIGURE 1 a, b, c

Figure 1a: RHDN+; Figure 1b: RHDN-; Figure 1c: NHP. Each figure shows the mean deviation (mm) of the subjective midpoint on the visual line bisection task as a function of OKS conditions (static, mixed, leftward, rightward). Zero indicates the correct midpoint. Negative values indicate shift to the left of the midpoint (i.e., leftward deviation), positive values indicate shift to the right of the midpoint (i.e., rightward deviation). Each error bar represents the standard error of the mean.

FIGURE 2 a, b, c

Figure 2a: RHDN+; Figure 2b: RHDN-; Figure 2c: NHP

Each figure shows the mean difference (d) between the observed (O) and the correct (C) responses (dO-C) as a function OKS conditions (static, mixed, leftward, rightward). Zero indicates correct responses. Negative values indicate shifts to the left of the correct response (i.e., underestimation) and positive values indicate shifts to the right of the correct response (i.e., overestimation). Each error bar represents the standard error of the mean.
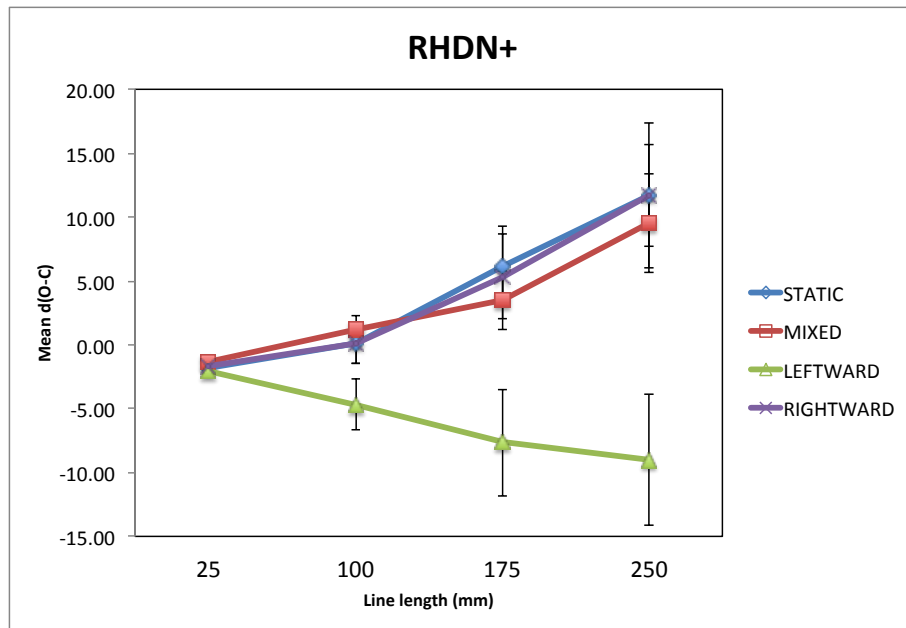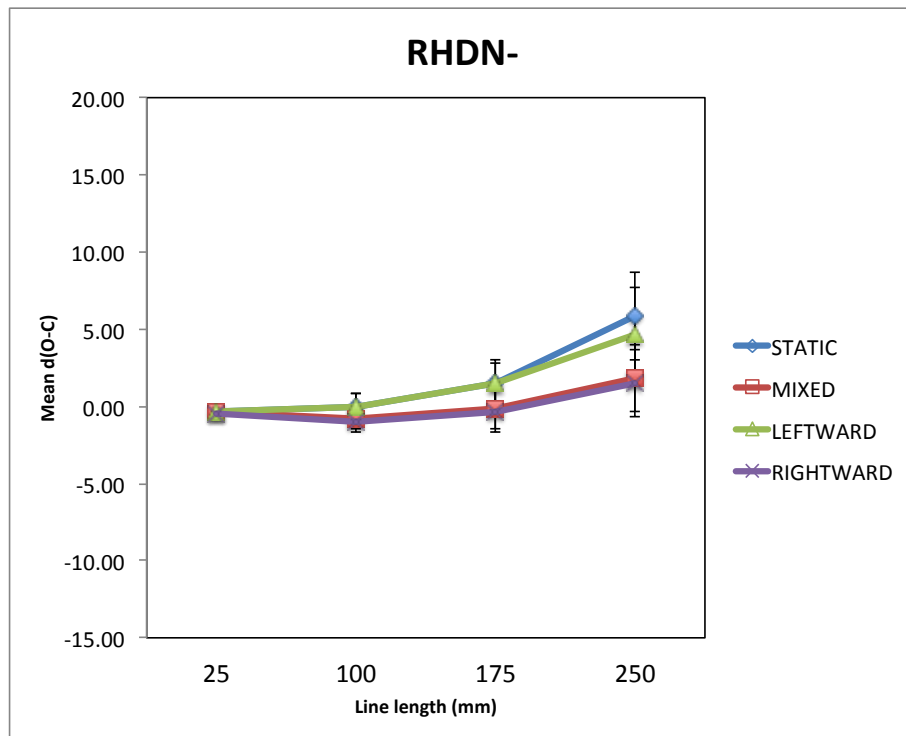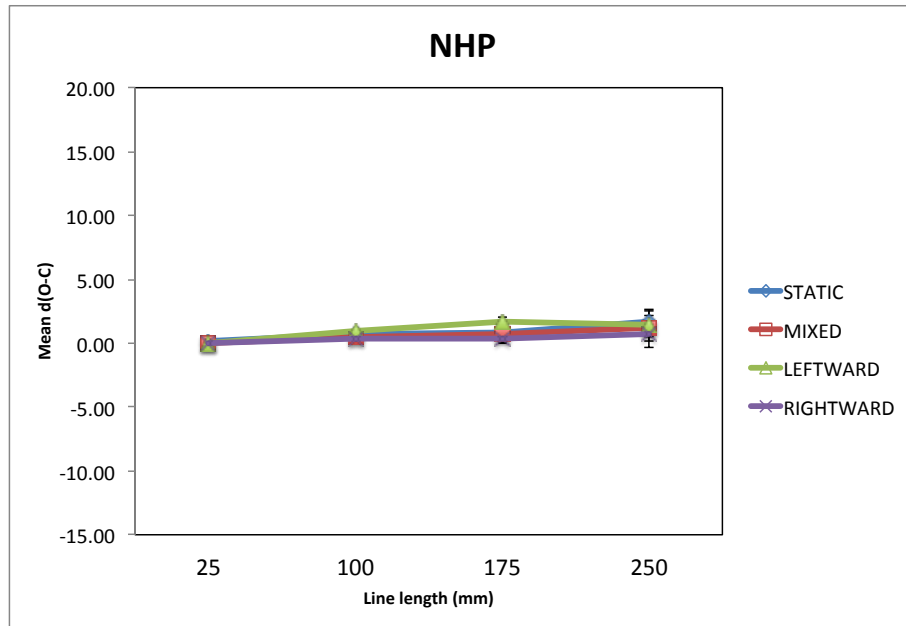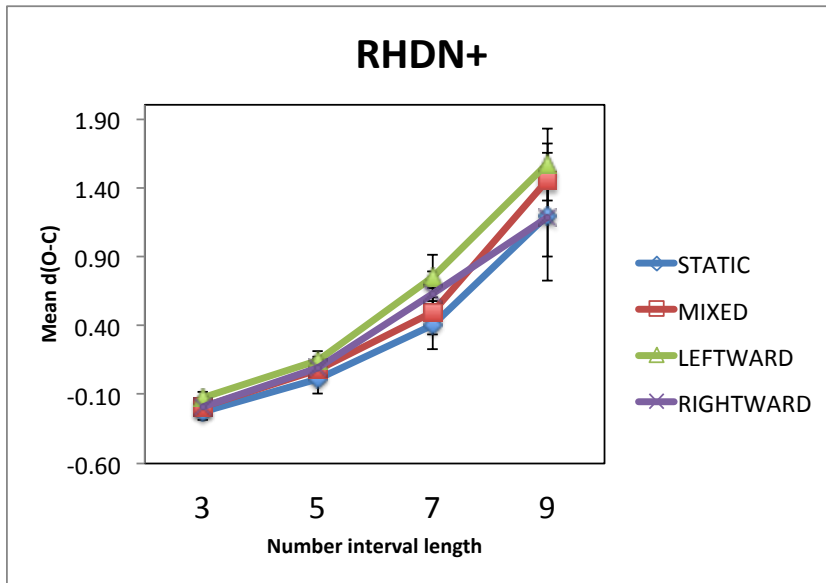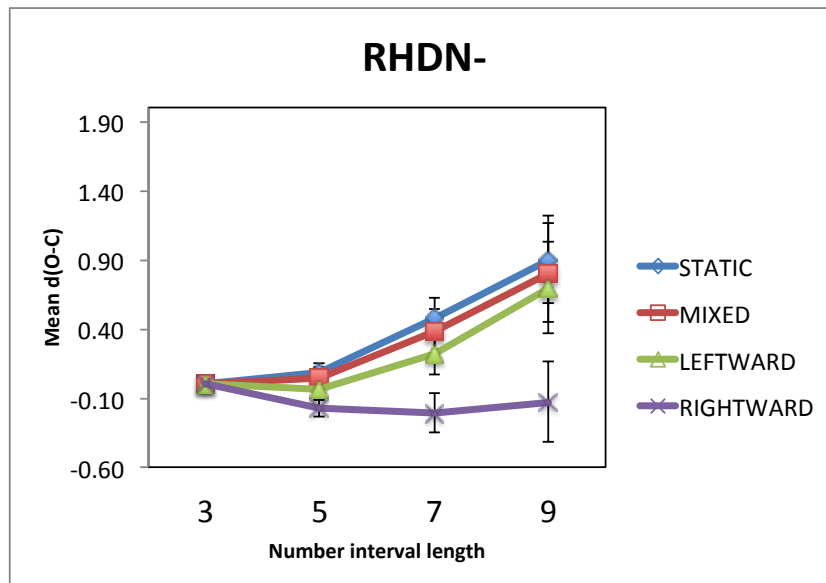
FIGURES

FIGURE 1a

FIGURE 1b

FIGURE 1c

FIGURE 2a

FIGURE 2b

FIGURE 2c