

Ipsilesional deficit of selective attention in left homonymous hemianopia and left unilateral spatial neglect

Sylvie Chokron, Carole Peyrin, Céline Perez

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Results. Results on accuracy showed that both LN and LH patients exhibited lower correct responses than Normal controls in their ipsilesional right visual field, suggesting an attentional deficit in their ipsilesional, supposed healthy visual field. More specifically, LH patients exhibited a specific deficit for processing single large stimuli, but not for processing flanked stimuli, relative to normal controls. LN patients exhibited lower correct responses for processing all types of stimulus than normal controls, but also than right brain damaged controls, in both visual fields suggesting a non-lateralized deficit not only due to the right hemisphere lesion. Furthermore, this deficit is more pronounced for flanked small stimuli, requiring higher attentional load. Conclusions The present results bring further evidence that patients with left homonymous hemianopia or left unilateral neglect both present a weaker but significant ipsilesional deficit in addition to their wellknown massive contralesional deficit. The presence of a specific attentional deficit in the right ipsilesional visual field of left hemianopic and left neglect patients is discussed regarding the hypothesis of hemispheric specialization for selective spatial attention and may have clinical implications for both conditions.

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Looking forward to hearing from you,

Yours sincerely,

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Highlights

- Presence of a weaker but significant ipsilesional deficit in left neglect and left hemianopic patients in addition to their well-known massive contralesional deficit
- Non lateralized deficit in left neglect patients linked to the attentional load of the task
- Specific attentional deficit in processing global stimuli in the ipsilesional visual field of left hemianopic patients (right brain-damaged)

Running Head: Ipsilesional Attention Deficit in hemianopia and neglect Ipsilesional Deficit of Selective Attention in Left homonymous hemianopia and Left Unilateral spatial Neglect Sylvie Chokron^{1,2}, Carole Peyrin³, and Céline Perez² ¹ Laboratoire de Psychologie de la Perception; UMR 8242 CNRS-Université Paris-Descartes, Paris, France ² Unité Vision et Cognition, Fondation Ophtalmologique A. de Rothschild; 25 rue Manin; 75019 Paris; France. ³ Univ. Grenoble Alpes, CNRS, LPNC UMR 5105, F-38000 Grenoble, France **Corresponding author:** Sylvie CHOKRON, LPP, UMR 8242, CNRS and Université Paris-Descartes and Unité Vision et Cognition, Fondation Ophtalmologique Rothschild, 25 rue Manin, 75019 Paris, France Tel: (33)-1-48-03-68-52 Fax: (33)-1-48-03-65-51 Email: sylvie.chokron@gmail.com

Abstract

Aims. Patients with homonymous hemianopia may present a subtle ipsilesional deficit, recently referred to as 'sightblindness' in addition to the contralesional visual field defect. We recently demonstrated that this deficit could be worse in right brain-damaged patients with left hemianopia than in left brain-damaged patients with right hemianopia, confirming right hemisphere dominance for visuo-spatial and attentional capacities. In the present study we investigate whether this ipsilesional deficit could be attentional in nature and to what extent it is comparable in right brain-damaged (RBD) patients with left hemianopia and in RBD patients with left neglect. The study was also conducted in RBD patients with neither left hemianopia nor left neglect signs in order to test if a right hemisphere lesion per se could be responsible for subtle ipsilesional attentional deficit. To reach this aim, we tested selective attentional capacities in both visual fields of 10 right brain-damaged patients with left neglect (LN), 8 right brain-damaged patients with no signs of left neglect or left hemianopia (RBD controls), and 17 healthy agematched participants (Normal controls).

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Keywords Homonymous hemianopia, Unilateral spatial neglect, sighblindness, hemispheric specialization, selective attention

1. Introduction

Participants suffering from left unilateral neglect are usually described as being impaired in responding to stimulation in the hemispace controlateral to the brain lesion (Heilman & Valenstein, 1979; for a review, see Bartolomeo & Chokron, 2000). In addition, it has been repeatedly demonstrated that patients do not simply neglect left objects but are also attracted by right ones (Mark et al., 1988; Marshall & Halligan, 1989). This behaviour has been interpreted as a 'rightward attentional capture' and indeed several experiments have demonstrated that reducing visual salience in the right hemispace may decrease left neglect signs (Mark et al., 1988; Marshall & Halligan, 1993; Chokron et al., 2004). The hypothesis of a rightward attraction of attention increasing left neglect behavior raises an important question: does the rightward bias reflect enhanced attention to the right hemispace? This assumption would fit several attentional models such as Kinsbourne's model (1970) predicting that there is a bias towards orienting attention in the rightward, ipsilesional hemispace of left neglect patients due to the release of left hemisphere from right hemisphere inhibition (see for discussion, Bartolomeo & Chokron, 2002). Along those lines, Làdavas et al. (1990), and subsequently Natale et al. (2007), found that right brain-damaged patients with left neglect may respond faster to ipsilesional targets than right brain-damaged patients without neglect or may even outperform healthy participants (in the latter study). More recently, Vossel and Fink (2016) found that in right brain-damaged patients, the presence of a distractor in the contralesional hemifield expedited ipsilesional (i.e., right) target detection. This effect was significantly related to lesions in the anterior middle temporal and temporoparietal cortex. external and internal capsule, as well as the superior longitudinal fascicle (SLF). The authors thus suggested that damage to the temporal and temporoparietal cortex and white matter tracts may transform contralesional stimulation into an unspecific saliency signal contributing to facilitating information processing in ipsilesional space. However, rather than being interpreted

in terms of facilitation, the rightward orientation of attention could be seen as a deficit in neglect patients. Indeed, according to Viken et al. (2014), the ipsilesional capture of attention in left neglect patients could be a predictor of chronic deficit. Indeed, these authors demonstrated that the most important predictors assessed early after stroke were presence of ipsilesional bias for dependency at 3 months and visual processing speed for dependency at 2 years after stroke. In this manner, the increase in rightward orientation of attention could be seen as a core deficit of unilateral spatial neglect.

Contrasting with the idea of a rightward facilitation, Bartolomeo and Chokron (1999), as well as Bartolomeo et al. (1999), found that left neglect patients were slower than normal controls when responding to left, but also to right, ipsilesional stimuli. This finding can be interpreted based on Heilman and Van den Abell's (1980) hypothesis that the left hemisphere attends only to contralateral space whereas the right attends to both contralateral and ipsilateral hemispaces. Thus, left hemispheric damage could be compensated for by right hemispheric attentional mechanisms, thereby only rarely provoking right neglect. Conversely, right cerebral damage would cause left neglect because the left hemisphere is unable to attend to the left hemispace. An essential corollary of this hypothesis is that right hemisphere lesions should determine a severe deficit in attention for the contralateral hemispace, but also a milder ipsilesional deficit, because fewer attentional resources could now be deployed in the right hemispace. Consistently, Bartolomeo and Chokron (1999) and Bartolomeo et al. (1999), found that left neglect patients were also impaired in their right hemispace. In addition, the authors demonstrated that this ipsilesional slowing of reaction times does not simply reflect a nonspecific arousal deficit, but is strictly related to the severity of left neglect. In addition, they demonstrated that the capacity to inhibit successive responses to right-sided events could predict performance on the left side of paper and pencil neglect tests (Bartolomeo et al., 1999). The rightward attentional bias in left neglect patients can thus take the form of a facilitation for simple detection as mentioned above or a deficit in more complex attentional tasks. Therefore, it seems to be one of defective, and not enhanced, attention, but the nature of this deficit is still unclear.

On the one hand, according to Robertson (1993; 2001), unilateral neglect would be very strongly associated with a fundamental loss of attentional capacity that may not be confined to one region of space, but could also involve the right ipsilesional space, meaning a nonlateralized attentional deficit. In this view, neglect patients suffer from a spatially nonselective component of attentional deficit that may be some form of basic arousal dysfunction. On the other hand, the attentional deficit in the ipsilesional field of left neglect patients could merely involve selective attention such as filtering processing. Indeed, using a 'flanker task' (e.g., the identification of a central stimulus flanked on both sides by task-irrelevant flankers), Snow and Mattingley (2006) clearly demonstrated that right brain-damaged patients with left unilateral neglect or extinction have a specific impairment in the ability to selectively inhibit taskirrelevant information within the ipsilesional visual field (IVF). Thus, according to these authors, in addition to the deficit of spatial orientation of attention present in left neglect patients, selective attention in IVF might more accurately be viewed as 'dysfunctional' rather than 'intact', as previously thought (for review, see Snow & Mattingley, 2006). Indeed, it has to be noted that although the orientation of attention in space has been extensively studied in left neglect patients (for review, see Bartolomeo & Chokron, 2002), relatively few studies have focused on selective attention. When they did, these studies mainly focused on the deficit in the left, contralesional hemispace (see for example, Rapcsak et al., 1989 and Lavie & Robertson, 2001), but not on the behaviour in the right, ipsilesional space. Interestingly, regarding visual field defects consecutive to retrochiasmatic unilateral damage (V1), the same conclusion can be drawn.

Indeed, most studies focused on the contralesional visual field, either on the deficit per se or on the residual, implicit capacities, referred to as 'blindsight' (Weiszkrantz, 2004). However, contrary to the case of blindsight, which has been extensively studied in hemianopic patients, vision quality in the central visual field and in the IVF of these patients has scarcely been assessed, and moreover, has traditionally been assumed to be fully preserved. Yet, regarding visuo-attentional capacities in the IVF of hemianopic patients, Hess and Pointer (1989) proposed that spatial and temporal sensitivities were lower than in control subjects. Rizzo and Robin (1996), followed by Poggel et al. (2011), confirmed that hemianopic patients can exhibit lower sensitivity to signals, compromised processing of temporal information and longer reaction times in both contralesional and ipsilesional visual fields, as compared to control participants. By studying a patient one week before and six months after a surgical intervention (embolization of an arteriovenous malformation in the right occipital lobe), we directly addressed the role of the right visual cortex on local analysis (based on the high spatial frequency content of scene stimuli) and global analysis (based on the low spatial frequency content) of visual information in scenes (Peyrin et al., 2006b). Results confirmed that damage to the right primary visual cortex (V1) induces a decrease in performance in the right IVF. In fact, the patient was found even before surgery to perform with lesser accuracy and higher reaction times in the right IVF for all types of scenes compared to performance in healthy controls and presented an additional deficit for global analysis (based on low spatial frequencies) in her right IVF after surgery. This study led us to hypothesize that the right occipital lobe could be involved in the processing of the global aspects of a visual scene (low spatial frequencies) in both visual fields. The right temporo-parietal junction has already been hypothesized to be involved in global processing (Fink et al., 1997, 1999).

Regarding visual detection and analysis, Paramei and Sabel (2008) reported that hemianopic patients exhibited diminished ability to detect fragmented targets among a noisy background in the IVF, whereas Schadow et al. (2009) found deficits in the early and late visual processing of Gestalt patterns in the IVF. More recently, Bola et al. (2013a) confirmed these findings and reported processing-speed deficits in a simple detection task in the IVF. The authors termed this phenomenon *sightblindness*, as the reverse situation of *blindsight* (Bola et al. 2013b): the former refers to visuo-attentional deficits in the IVF, whereas the latter refers to residual (although implicit) visual abilities in the controlateral visual field (CVF) that are highlighted in forced-choice tasks (e.g., Weiskrantz et al., 1974; Leopold, 2012). Along those lines, and as recently suggested, neither the central visual field (Cavézian et al., 2010; 2015; Perez et al., 2013) nor the IVF of hemianopic patients (Bola et al., 2013a; 2013b; Sanchez-Lopez et al., in press) actually appear to be fully intact or functional. In line of these findings, it was also demonstrated that cortical reorganization may be observed not only in the lesioned but also in the healthy hemisphere after a unilateral occipital damage acquired in childhood (Mikellidou et al., in press). Moreover, as we proposed, the nature of the task and the type of stimulus may determine the central and ipsilesional visual deficit and the pattern of cortical activation of hemianopic patients (Cavézian et al., 2010, 2015; Perez et al., 2013, Chokron et al., 2016). As a matter of fact, recently, we specifically investigated the effect of lesion side on the nature and severity of the ipsilesional deficit (Cavézian et al., 2015). In this study, five left and five right hemianopic patients were presented filtered (high or low spatial frequencies) as well as non-filtered scenes in their IVF during a detection and a categorization task. Right braindamaged patients with left hemianopia made more errors for categorizing scenes in their IVF than did their matched controls, regardless of the spatial frequency content of scene. In contrast, left brain-damaged patients with right hemianopia made more errors than did the controls only when categorizing high spatial frequency scenes. Interestingly, in both tasks (detection and categorization), the right brain-damaged patients performed worse in their IVF than did the left brain-damaged patients.

Together, these studies among right brain-damaged patients suffering either from left neglect or left homonymous hemianopia raise the question of the integrity of selective attention processing in the ipsilesional healthy right visual field. However, most of the studies among both LN patients and LH patients focused mainly on selective attention in the contralesional and not ipsilesional visual field. Indeed, authors focused either on the disentangling between LH and LN (Walker et al., 1991; Nadeau & Heilman, 1991; Ferber & Karnath, 2001; Müller-Oehring et al., 2003) or on the additive effect of LN and LH in processing stimuli in the contralesional field (Doricchi & Angelelli, 1999; Barton, Behrmann and Black, 1998; Saj et al., 2012), whereas other studies aimed to investigate how these two types of patients react to nonvisual stimuli (Kerkhoff, Artinger, & Ziegler; 1999; Bolognini et al, 2016). Only a few studies were interested in comparing the behavior of LN and LH patients in their ipsilesional visual field (Barrett, Peterlin, & Heilman, 2003; Tant et al., 2002; Gainotti et al., 2009: Doricchi et al., 2005).

The aim of the present study was thus to investigate the presence, the nature and the severity of a selective spatial attention deficit in the ipsilesional visual field of both LN and LH patients and to understand to which extent the nature of the deficit in the contralesional visual field (attentional or visual) could determine the nature of the ipsilesional attentional deficit. The concept of selective spatial attention usually refers to the ability to focus on areas of visual space to facilitate target detection (Posner & Petersen, 1990). According to many authors, the key notion in selective attention is a filtering process that ensures amplification of the target and/or attenuation of background information (Broadbent, 1958; Kahneman & Treisman, 1984; Shiffrin & Czerwinski 1988). In the present study, we used a letter-detection task (Chokron et al., 2000; Tabert et al., 2000) to test if right brain-damaged patients suffering from either left unilateral spatial neglect (LN) or left homonymous hemianopia (LH) may present a deficit of selective attention, in their right ipsilesional visual field as compared to normal controls.

By previously using this task in healthy volunteers, we were able to demonstrate that when selective attention is required to identify a visual target surrounded by flankers, reaction times (RTs) are shorter in the right than in the left visual field (Chokron et al., 2000; 2003; Buchsbaum et al, 2006), thus confirming a left hemisphere (LH) advantage for filtering irrelevant information and analyzing the local features of a visual scene (Robertson & Lamb, 1991; Robertson et al., 1988). Conversely, RTs were found to be shorter in the left visual field (LVF) than in the right visual field (RVF) when the target to be identified was presented alone and required less filtering activity (i.e. less selective attention). We thus demonstrated a left hemisphere (LH) specialization for selective attention and a right hemisphere (RH) specialization for global visual detection. According to these results, a number of predictions can be made regarding the performance of left neglect and left hemianopic patients while performing the present task: (1) If left neglect patients and left hemianopic patients present an attentional deficit in their ipsilesional field, we should observe lower performance in their right IVF as compared to controls' performance; (2) If the right occipital lobe is specifically involved in the global processing of visual information in both hemifields, as we previously hypothesized, we should observe a specific deficit for big stimuli (global processing) in the right IVF of left hemianopic patients as compared to controls' performance; (3) If there is a more general non-lateralized deficit of arousal in left neglect patients, as suggested for example by Robertson (2001), performance in both visual fields (RT and accuracy) should be worse for all types of stimuli (with high or low attentional demand) compared to controls; (4) If this nonlateralized arousal deficit is specifically linked to the neglect syndrome, and not a consequence of the right hemisphere lesion, performance should be worse for all types of stimuli in both visual fields compared to right brain damaged controls; (5) If the non-lateralized attentional deficit of LN patients is linked to the attentional load, we should observe, in both visual hemifields, lower performance when processing small stimuli surrounded by flankers than large stimuli presented alone.

2. Material and Methods

Participants

Seventeen healthy, dextral, male adults (Normal controls); age range 52 to 77 years; M = 60.2, SD = 7.94), eight right brain-damaged male patients with no sign of left hemianopia or left unilateral spatial neglect (RBD patients; age range 53 to 79 years; M = 63.7; SD = 12.87), ten right brain-damaged male patients diagnosed with left unilateral spatial neglect (LN patients; age range 46 to 69 years; M = 58.8; SD = 6.61), and eight right brain-damaged male patients with a right occipital lesion and diagnosed with left homonymous hemianopia (LH patients; age range 48 to 72 years; M = 63, SD = 8.24) participated in the study.

Unilateral Spatial Neglect was assessed using the BEN (Batterie d'évaluation de la Négligence; Azouvi et al., 2002). Visual field defects were diagnosed using the BEN in all patients and confirmed with automatic perimetry in hemianopic patients (see Table 1 and Figure 1). All participants (controls and patients) had normal or corrected-to-normal vision (acuity), left-to-right reading habits, and used the Roman alphabet. Demographical and clinical data are detailed in Table 1.

/Insert Table 1/

/Insert Figure 1/

Stimuli and Procedure

Stimuli were either the letter O, the letter C, or the digit zero (0) appearing either alone as a large character (single large condition) or as a small character surrounded by eight other letters (the letter G or Q, flanked small condition; see Figure 2). The overall size of the stimuli was controlled so that the large letters were of the same dimensions as the pattern of small letters surrounded by flankers (19 mm wide \times 22 mm high). Each trial began with a central fixation cross that was presented for 300 ms (in order to control the gaze direction to the center of the screen), and remained during the presentation of the stimulus displayed during 150 ms in either the left visual field (LVF) or the right visual field (RVF) at 2° from a fixation dot. Participants performed a lateralized letter-detection task. The task consisted of pressing a button with the right hand only when detecting a target (large or small O) and to ignore the trials where a distractor was flashed (0 or C) (see Tabert et al., 2000 for complete procedure). The experiment contained 128 trials (16 LVF single large target, 16 RVF single large target, 16 LVF flanked small target, 16 RVF flanked small target, 16 RVF flanked small distractor). Response accuracy and response times (in milliseconds) were recorded for each trial.

/Insert Figure 2/

3. Results

/Insert Table 2/

Correct responses (CR)

An ANOVA was performed on mCR (Table 2 and Figure 3) with Group (Normal controls, RBD, LN, and LH) and Visual field (LVF and RVF) as a between-subjects factors

and Stimulus type (single large and flanked small) as a within-subject factor. The ANOVA revealed a main effect of Group ($F_{3,39} = 28.15$, p < 0.0001), Visual hemifield ($F_{1,39} = 50.33$, p < 0.0001), and Stimulus type (F_{1,39} = 103.7, p < 0.0001), but the interaction Group \times Visual field \times Stimulus Type was not significant (F_{3,39} < 1). A priori specific hypotheses were tested using contrast analysis with modified Bonferroni-corrected alpha value ($\alpha_{adjusted}$) for nonorthogonal comparisons. We first hypothesized that LN and LH patients would present a deficit of selective attention in their ipsilesional field in comparison with NC. Indeed, when stimuli were displayed in the ipsilateral RVF, the mCR was significantly lower for LN ($51.6 \pm 21.9\%$) and LH (62.1 \pm 28.5%) than NC (77.2 \pm 20.3%; F_{1,39} = 12.61, p < 0.001, $\alpha_{adjusted}$ = 0.033 for all 3 possible pairwise comparisons; residual effect: $F_{1,39} = 1.73$, p = 0.20). Then, to test a specific deficit for LH patients to process global information relative to local information in the ipsilateral RVF, we directly compared mCR between LH and NC on each stimulus type. For single large stimuli, the mCR was significantly lower for LH (70.3 \pm 31.8%) than NC (98.7 \pm 8.5%; $F_{1,39} = 7.28$, p < 0.01). For small flanked stimuli, there was no difference between LH $(53.9 \pm \%)$ and NC (64.7 ± 16.8%; F_{1,39} = 1.37, p = 0.25). Concerning more specifically LN patients, we tested the hypothesis of a non-lateralized attentional deficit in LN patients by comparing mCR between LN and NC irrespective of the visual field. The mCR was significantly lower for LN (45.2 \pm 21.2%) than NC (78.9 \pm 18.3%; F_{1.39} = 44.21, p < 0.001). To test if the non-lateralized attentional deficit is only a consequence of the right hemisphere lesion, we directly compared mCR between LN and RBD. The mCR was significantly lower for LN than RBD (67.4 \pm 24.8%; F_{1.39} = 13.49, p < 0.001). Finally, we tested if the attentional deficit is linked to the attentional load by comparing mCR between the two types of stimuli in both visual fields. The mCR was significantly lower for flanked small stimuli $(33.1 \pm 20.6\%)$ than single large stimuli (57.2 \pm 13.8%; F_{1,39} = 25.6, p < 0.001).

/Insert Figure 3/

Reaction times (RT)

As presented in Table 2, mCR of LH patients is very low in the left visual hemifield, i.e. their blind contralesional visual field, causing the absence of mean correct reaction times (mRT) for 7 out of 8 patients. Thus, only mRT in the right visual hemifield (i.e. healthy ipsilesional visual field for LN, LH and RBD patients; Figure 4) were analyzed. An ANOVA was performed on mRT with Group (Normal controls, RBD, LN, and LH) as a between-subjects factors and Stimulus type (single large and flanked small) as a within-subject factor. The ANOVA showed a main effect of Stimulus type ($F_{1.39} = 13.25$, p < 0.001), with small stimuli surrounded by flankers eliciting longer RT than large stimuli presented alone. We found neither a main effect of Group ($F_{3,39} = 1.15$, p = 0.34), nor a significant Group \times Stimulus Type interaction ($F_{3,39} = 1.06$, p = 0.38). A priori specific hypotheses were here tested when concerning the right visual hemifield only, using contrast analysis with modified Bonferronicorrected alpha value ($\alpha_{adjusted}$) for non-orthogonal comparisons. The mRT did not significantly differ between LN (532 \pm 123 ms), LH (493 \pm 129 ms) and NC (470 \pm 90 ms; F_{1,39} = 12.61, p < 0.001, $\alpha_{adjusted} = 0.033$ for 3 possible pairwise comparisons). Then, there was no significant difference between LH and NC, for neither single large stimuli (476 \pm 135 ms and 429 \pm 82 ms, respectively; $F_{1,39} = 1.12$, p = 0.30) nor flanked small stimuli (509 ± 129 ms and 513 ± 80 ms, respectively; $F_{1,39} > 1$). Finally, there was no significant difference between LN (532 ± 123) ms) and RBD (527 \pm 101 ms; F_{1,39} < 1).

/Insert Figure 4/

4. Discussion

The present study investigated a possible selective attention deficit in the right, ipsilesional visual field of right brain-damaged patients suffering either from left neglect or left hemianopia.

In fact, our findings demonstrate a significant difference in performance between control participants and LH and LN patients. Indeed, when stimuli were displayed in the ipsilateral right visual field, LN and LH patients presented lower performance than healthy controls (NC). More specifically, LH patients presented significantly lower performance in detecting a large visual stimulus, but not a flanked small stimulus, in their ipsilesional visual field compared to NC. LN patients, for their part, presented lower performance than NC, but also than RBD controls, in detecting all type of stimulus in both visual hemifields. The present findings bring evidence for the presence of a non-lateralized attentional deficit in LN patients that cannot be attributed solely to the presence of right brain damage, as well as a subtle attentional deficit in the ipsilesional visual field of LH patients and are discussed below regarding models of neglect and homonymous hemianopia.

Ipsilesional attentional bias in left neglect patients

The present paper confirms previous findings emphasizing the presence of an ipsilesional spatial bias in RBD patients suffering from left neglect that, according to some studies may be correlated to the lateralized contralesional deficit of these patients (Rusconi et al., 2002; Battelli et al., 2001; Bartolomeo & Chokron, 1999; Bartolomeo et al., 1999; Robertson, 2001). As pointed out by He et al., (2007) previous studies on healthy subjects indicate that the dorsal network mediates control of spatial attention with a contralateral bias (Corbetta et al., 2000, 2002; Macaluso et al., 2002; Sereno et al., 2001; Silver et al., 2005), while the ventral system is involved in nonlateralized attentional functions, including spatial and temporal capacity (Husain & Rorden, 2003; Peers et al., 2005; Shapiro et al., 2002)

vigilance (Pardo et al., 1991), saliency detection (Serences et al., 2004), and reorienting of attention (Corbetta et al., 2000; Macaluso et al., 2002; Carter et al, 2016). Along these lines and as highlighted by He et al. (2007), neglect patients may show both spatially lateralized and nonlateralized deficits, as seen here, because of the interaction between structural and functional damage to the ventral and dorsal frontoparietal attention networks. Recent studies dealing with the neuroanatomy of neglect signs in RBD patients revealed that specific neural correlates could be put forward for the different components including the right inferior parietal lobule for the perceptive/visuo-spatial component, the right dorsolateral prefrontal cortex for the exploratory/visuo-motor component, deep temporal lobe regions for the allocentric/objectcentred component whereas subcortical damage to paraventricular white matter tracts was associated with severe neglect encompassing several tests (Verdon et al., 2010). However, in this model, the presence of an ipsilesional deficit was not specifically looked for and correlated to specific neuroanatomical damage. Nevertheless, in a recent investigation of structural whitematter mediating left neglect components in RBD patients, Vaessen et al. (2016) suggested that posterior parts of the superior longitudinal fasciculus (SLF), as well as nearby callosal fibers connecting ipsilateral and contralateral parietal areas, were associated with perceptual spatial deficits, whereas more anterior parts of SLF and inferior fronto-occipital fasciculus (IFOF) were predominantly associated with object-centered deficits in left neglect patients. Along those lines, a damage to the nearby callosal fibers connecting ipsilateral and contralateral parietal areas could easily explain the ipsilesional deficit that can be found, as in the present experiment, in left neglect patients. Further studies are needed to investigate the specific neuroanatomical correlates of this ipsilesional deficit.

From a functional viewpoint, regarding our predictions expressed in the Introduction, the presence of an ipsilesional deficit for both small and large targets in left neglect patients is compatible with a general non-lateralized attentional deficit. In addition, the fact that this deficit is more salient (in terms of correct responses) in the condition with a high attentional load (for small rather than large stimuli) than in global visual detection could indicate that the type of attentional processes required may also have an effect on this non-lateralized deficit confirming He and co-workers' (2007) model of an interaction between the dorsal and the ventral attentional systems. The present study confirms and extends Rapcsak and coworkers' (1989) findings in showing that increasing demands on visual selective attention adversely affects left neglect patients' performance in both hemifields. From a clinical point of view, the fact that the attentional load significantly modulates the ipsilesional deficit highlights the necessity of diagnosing neglect signs and attentional deficits using a battery of tests. In fact, it has been repeatedly found that tasks requiring selective attention are more suitable in revealing neglect signs than simple detection tasks (see for example Azouvi et al., 2002). Importantly, the fact that LN patient performance is significantly lower than healthy controls and RBD controls underline that this non-lateralized deficit cannot be attributed solely to the presence of a right brain damage.

Ipsilesional attentional bias in left hemianopic patients

In line with previous studies (Rizzo & Robin, 1996; Peyrin et al., 2006a; Bola et al., 2013b; Cavezian et al., 2015), we confirmed that a unilateral right visual cortex lesion produces ipsilesional visuo-attentional deficits at least for large stimuli. There are both anatomical and functional arguments to explain this finding.

Historically, from an anatomical point of view, it was established in the last century that the deficit caused by a unilateral occipital lobe lesion was restricted to the controlateral visual field and led to the assumption that there is a consistent relationship between visual field defects and loci of brain damage in the calcarine cortex, (i.e., Brodmann's area 17 or VI). However, according to Rizzo and Robin (1996), even after a lesion of the primary visual cortex (V1), VI dysfunction is unlikely to occur in isolation in human cases. Rather, extrastriate dysfunction, contralesional dysfunction, and/or parietal dysfunction resulting in attentional disorders should generally co-occur, as demonstrated here.

From a functional point of view, primate extrastriate areas receive extensive visual inputs from both ipsi- and contralateral hemispheres (Rockland, 1994). They also contain neurons with receptive fields that overlap the vertical meridian (Desimone et al., 1993) and neurons whose activity is modulated during attention tasks (Moran & Desimone, 1985; Spitzer et al.1988; Logothetis & Schall, 1989; Schiller & Lee, 1991). Comparative anatomo-functional evidence suggests that similar neurons and connections exist in humans, and human visual cortex activity appears to be attention-dependent (Corbetta et al., 1991; Sengpiel & Hübener, 1999; Somers et al., 1999). Taken together, this anatomical and functional evidence explains that a unilateral human visual cortex lesion may reduce visual performance (accuracy and speed) in both hemifields. This explanation is in line with both the interhemispheric diaschisis effects put forward early last century, as well as attention-related deficits. Consequently, our results are in accordance with studies showing that the useful visual field of view in patients with homonymous hemianopia after a unilateral occipital lesion may be bilaterally constricted (Ball et al., 1993).

Although the specific mechanisms responsible for ipsilesional visual deficits in hemianopic patients remain to be clarified, several explanations have been proposed. First, Rizzo and Robin (1996) interpreted these global effects of a unilateral occipital lesion in terms of a limited capacity attention model (Broadbent, 1958). According to this model, damage to a portion of the visual cortical pathways reduces information processing capacity and efficiency of the whole system. More recently, Bola et al. (2013b) proposed that weaker and delayed activation in the injured hemisphere might compromise inter-hemispheric interactions and alter synchronization of the non-lesioned hemisphere to induce subtle visual deficits in the IVF. The present findings reinforce the premise that the side of the occipital lesion can influence the pattern of interhemispheric desynchronization.Indeed, given the evidence of hemispheric specialization for visual processing, we recently hypothesized that the side of the occipital lesion could indeed have specific effects on interhemispheric desynchronization (Cavezian et al., 2010; 2015; Perez et al., 2013).

Finally, Dai et al. (2013) recently hypothesized and Bola et al. (2013b, 2014) recently discussed the premise that the occipital lesion and its functional consequences (loss of the contralesional visual field) lead to widespread changes in the brain. In addition, Bola et al. (2014) proposed that vision loss in blind subjects after a peripheral lesion is caused not only by primary tissue damage but also by a breakdown of synchronization in brain networks. Thus, evidence has emerged that there is a complex and widespread reorganization of long-range brain networks following peripheral or cortical visual impairment. Indeed, as recently pointed out by Lanyon and Barton (2013), deficits in homonymous hemianopia after unilateral damage to the primary visual cortex might also vary across time, with more attentional deficits at the acute phase than after a few months.

In addition, in the present study, right brain-damaged patients with left hemianopia show a specific deficit in processing large stimuli and no deficit for local processing in their right ipsilesional visual field. This finding confirms previous results showing right hemisphere dominance for global processing (Chokron et al., 2000) and raises the question of a hemispheric specialization for visuo-spatial processing at the occipital level as we recently proposed (Cavezian et al., 2010; 2015; Perez et al., 2013). As a matter of fact, this asymmetry between the left and right hemisphere has mostly been interpreted in terms of a superiority of the right hemisphere for the detection of simple visual stimuli. However, as underlined by Marzi et al (1991), this could also be interpreted as related to an asymmetry of interhemispheric transmission of visuomotor information, with transfer from the right hemisphere (side of stimulus entry) to the left (side of response generation) faster than in the reverse direction. Interestingly, the role of the corpus callosum in patients with unilateral lesions has been emphasized these past years. Indeed, in addition to the recent data showing that blindsight relies on an intact patway between the LGN and MT (see for review and discussion, Tamietto and Morrone, 2016), Celeghin and colleagues (2017) recently demonstrated in one patient with early primary visual cortex damage that blindsight and in particular the fact that HH patients can act on targets they do not consciously perceive could depend partly on the compensatory activity of the intact hemisphere, which can be dynamically recruited through the corpus confirm findings callosum. These data previous showing changes in anatomical connectivity between the damaged and the non-damaged hemisphere abovementioned. In addition, as Silvanto, Walsh and Cowey demonstrated, conversely to what is observed in healthy participants, applying TMS over the extrastriate area V5/MT+ in a HH patient' damaged hemisphere (GY) modulates the appearance of phosphenes induced from V1 in hemisphere. findings confirm the normal These an abnormal functional connectivity between V5/MT in the damaged hemisphere and the early visual cortex in the normal hemisphere, consistent with HH patients' abnormal anatomical connectivity between the two hemispheres.

Right hemisphere dominance for visuo-spatial processing in both visual fields

The hypothesis that the right occipital lobe dominates in visuo-spatial processing in the entire visual field parallels the well-described superiority of the right parietal lobe in spatial organization over the entire extra-personal space (Heilman & Van Den Abell, 1980) as well as the recurrent finding that left neglect after right cortical damage is more severe and more frequent than right neglect after left lesion (for review, see Bartolomeo & Chokron, 2002).

According to the present findings, right hemisphere dominance for attention would account for bilateral attentional deficits not only following parietal lesions as discussed above, but also following occipital lesions as found in the present study.

Interestingly, we recently demonstrated that in hemianopic patients, the deficit in the central and in the ipsilesional visual field is more marked in right brain-damaged patients than in left brain-damaged patients, suggesting that the dominance of the right hemisphere for visuo-spatial processing influences the severity of the deficit in both hemifields (Cavezian et al., 2010; 2015). In addition, we were able to show that the lesion side might also play a role in cortical reorganization after an occipital lesion (Perez et al., 2013). Indeed, during a visual categorization task performed in the central visual field, whereas left brain damaged patients with right hemianopia showed activation predominantly in their right hemisphere (namely, in their occipital lobe and posterior temporal areas), right brain damaged patients with left hemianopia showed a more bilateral activation (in their occipital lobes).

Taken together, the present findings as well as previous results further corroborate the superiority of the right hemisphere in visual processing recently discussed in normal controls using EEG (Le et al., 2015). Given right hemisphere superiority for visuo-spatial, and especially for global visual processing, a right occipital lesion would thus induce a loss of visual perception in the contralesional visual field (hemianopia) and an ipsilesional visuo-attentional deficit more marked for large visual stimuli processing as reported here.

Conclusions

The present findings emphasize the need to thoroughly test for visuo-attentional capacities in the assumed 'healthy' ipsilesional visual field of patients suffering from unilateral spatial neglect or homonymous hemianopia following unilateral parietal or occipital damage. Contralesional visual field training in rehabilitation is nearly always recommended for these patients. However, the present study clearly demonstrates that right brain-damaged patients with either left neglect or right hemianopia may present an ipsilesional visuo-attentional deficit as well. In addition, and as discussed above, the nature of the ipsilesional deficit seems to be dependent upon the pathological condition (left hemianopia vs left neglect) and could thus be dependent upon the specific location of cerebral damage. As a matter of fact, recently, blindsight has been hypothesized to depend partly upon the interaction between the damaged and the non-damaged hemisphere (Celeghin et al, 2015; 2017; Silvanto, Walsh and Cowey, 2009), the present findings suggest that this could also be the case for ipsilesional deficits in patients with unilateral parietal or occipital lesions.

Consequently, further studies should focus on the nature and severity of ipsilesional attentional deficits, both in homonymous hemianopia and in unilateral spatial neglect in relation with the side and site of brain damage, to establish if this bilateral deficit is mainly due to right hemisphere dominance for visuo-attentional processing or if this could be due to inter and intrahemispheric cortico-subcortical connectivity. This is of importance given the role of attention both in increasing sensitivity and awareness in hemianopic patients (Vernet et al., in press).

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Pathology ^a	Age	Sex⁵	Onset (days)	Years of schooling	Aetiology ^c	Lesion Localisation ^d	Visual Assessment (BEN) Unilateral (/4) and bilateral (/2) scores
NC	52	М		12			
NC	52	М		17			
NC	53	М		15			
NC	55	М		10			
NC	55	М		10			
NC	55	М		15			
NC	55	М		8			
NC	58	М		11			
NC	58	М		9			
NC	60	М		8			
NC	60	М		10			
NC	61	М		16			
NC	61	М		15			
NC	63	М		17			
NC	73	М		15			
NC	76	М		12			
NC	77	М		13			
LN	62	М	151	8	Haemorragic	TP	4/4 1/2
LN	55	М	149	12	Haemorragic	TP	3/4 2/2
LN	65	М	210	8	Haemorragic	TP	4/4 1/2
LN	69	М	445	17	Ischemic	Р	4/4 1/2
LN	60	М	86	6	Haemorragic	FP	4/4 1/2
LN	62	М	57	10	Haemorragic	FP	3/4 1/2
LN	61	М	449	11	TBI	Р	4/4 1/2
LN	54	М	139	16	Haemorragic	TP	4/4 1/2
LN	46	М	131	11	TBI	Р	4/4 1/2
LN	54	М	111	12	Haemorragic	TP	4/4 1/2
LH	55	М	320	6	Haemorragic	0	2/4 0/2
LH	48	М	620	15	Haemorragic	0	2/4 0/2
LH	60	М	350	8	Haemorragic	0	2/4 0/2
LH	65	М	420	11	Haemorragic	0	2/4 0/2
LH	65	М	450	17	Ischemic	0	2/4 0/2
LH	68	М	190	8	Ischemic	PO	2/4 0/2
LH	71	М	650	6	Haemorragic	0	2/4 0/2
LH	72	М	900	8	Haemorragic	PO	2/4 0/2
RBD Control	66	М	120	6	Haemorragic	IC,BG	4/4 2/2

Table 1: Demographic and clinical data

RBD Control	54	М	390	18	Ischemic	IC,BG	4/4 2/2
RBD Control	53	М	303	9	Haemorragic	IC,Th	4/4 2/2
RBD Control	68	М	250	16	Ischemic	FP	4/4 2/2
RBD Control	66	М	70	6	Haemorragic	FP	4/4 2/2
RBD Control	79	М	190	17	Haemorragic	F	4/4 2/2
RBD Control	61	М	135	23	Haemorragic	IC,Th	4/4 2/2
RBD Control	63	М	49	8	Ischemic	FP	4/4 2/2

^a: NC: Normal Control; LN: Left Neglect; LH: left homonymous hemianopia; RBD Control: Right brain damaged patients without left neglect and left homonymous hemianopia. ^b: M: Male. ^c: F: Frontal; T: Temporal; P: Parietal; O: Occipital; Th: Thalamus; IC: Intern Capsula; BG: Basal Ganglia; ^d:TBI: traumatic brain injury. **Table 2:** Mean percentage of correct responses (mCR) and standard deviation (SD) and mean correct reaction time in ms (mRT) and SD in the left and right visual hemifields for the two stimulus types (flanked small and single large stimuli) and all groups (Normal controls, right brain-damaged/RBD patients, left neglect patients, left hemianopic patients).

		-	Normal controls	Left Neglect patients	Left Hemianopic patients	RBD patients	
Left visual field	Flanked small	mCR (SD) mRT (SD)	69.9 (14.9) 522 (104)	26.9 (17.7) 615 (163)	1.6 (2.9) 516* (42)*	51.6 (19.7) 571 (124)	
	Single large	mCR (SD) mRT (SD)	94.5 (8.2) 419 (75)	50.6 (16.3) 564 (36)	14.1 (8.7) 453** (54)**	85.1 (11.6) 502 (56)	
Right visual field	Flanked small	mCR (SD) mRT (SD)	64.7 (16.8) 512 (80)	39.4 (23.6) 545 (117)	53.9 (24.1) 509 (129)	50.0 (25.4) 562 (120)	
	Single large	mCR (SD) mRT (SD)	89.7 (8.5) 429 (82)	63.8 (11.3) 518 (133)	70.3 (31.8) 476 (135)	82.8 (14.8) 493 (68)	

*mRT and SD calculated on 2 LH patients

**mRT and SD calculated on 7 LH patients

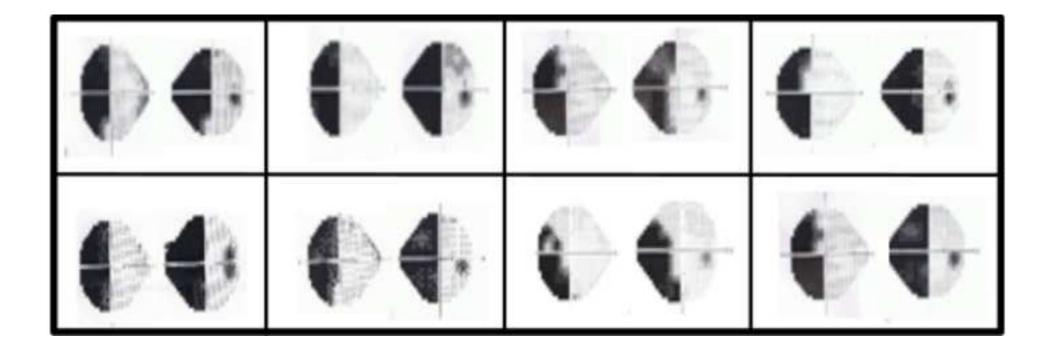
Figure Captions

Figure 1: Visual field examination (Humpreys 24-2) for hemianopic patients. In each box the visual field for the left eye and the right eye are presented.

Figure 2: Examples of stimuli displays. (a) The target can be a small letter o surrounded by flankers (top) or a large letter O presented alone (bottom). (b) In half of the trials, the letter C or the digit zero (0) were presented as distractors. As for targets, half of the distractors were presented surrounded by flankers (top) and the other half alone (bottom). Each type of stimulus (target or distractor, alone or surrounded by flankers) was presented equally in the left and right hemifield.

Figure 3: Percentage of correct responses as a function of the visual field (left visual field: LVF; right visual field: RVF), the groups (17 Normal controls: NC, 10 left neglect patients: LN, 8 left hemianopic patients: LH, 8 right brain-damaged controls: RBD), and the stimulus types (flanked small and single large stimuli). Error bars correspond to 95% confidence intervals.

Figure 4: Mean correction reaction times (in ms) in the right visual hemifield as a function of the groups (17 Normal controls: NC, 10 left neglect patients: LN, 8 left hemianopic patients: LH, 8 right brain-damaged controls: RBD) and the stimulus types (flanked small and single large stimuli). Error bars correspond to 95% confidence intervals.





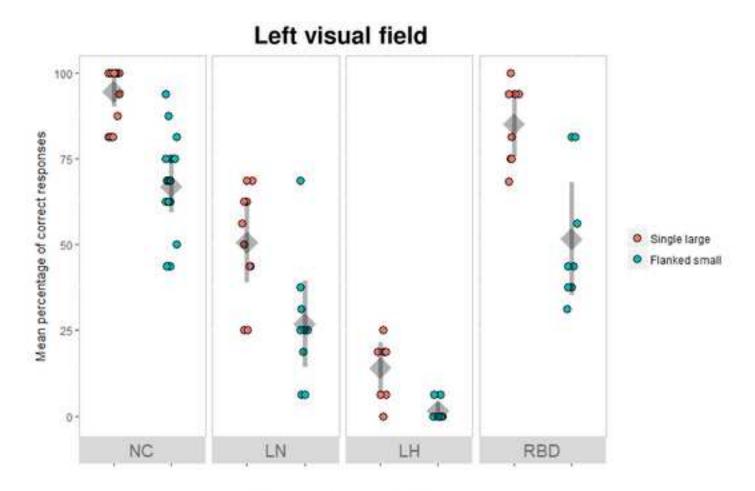
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Figure3Rev2 Click here to download high resolution image



Right visual field

