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► **To cite this version:**

Monica N. Toba, Raffaella Migliaccio, Alexia Potet, Pascale Pradat-Diehl, Paolo Bartolomeo. Right-Side Spatial Neglect and White Matter Disconnection after Left-Hemisphere Strokes.. *Brain Structure and Function*, 2022, 227 (9), pp.2991-3000. 10.1007/s00429-022-02541-7 . hal-03749909

HAL Id: hal-03749909

<https://u-picardie.hal.science/hal-03749909v1>

Submitted on 13 Sep 2024

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Right-side spatial neglect and white matter disconnection after left-hemisphere strokes

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Received: 15 February 2022 / Accepted: 17 July 2022

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Abstract

Spatial neglect usually concerns left-sided events after right-hemisphere damage. Its anatomical correlates are debated, with evidence suggesting an important role for fronto-parietal white matter disconnections in the right hemisphere. Here, we describe the less frequent occurrence of neglect for right-sided events, observed in three right-handed patients after a focal stroke in the left hemisphere. Patients were tested 1 month and 3 months after stroke. They performed a standardized paper-and-pencil neglect battery and underwent brain MRI with both structural and diffusion tensor (DT) sequences, in order to assess both grey matter and white matter tracts metrics. Lesions were manually reconstructed for each patient. Patients presented signs of mild right-sided neglect during visual search and line bisection. One patient also showed pathological performance in everyday life. Structural MRI demonstrated left parietal strokes in two patients, in the region extending from the postcentral gyrus to the temporo-parietal junction. One of these two patients also had had a previous occipital stroke. The remaining patient had a left frontal stroke, affecting the precentral, the postcentral gyri and the basal ganglia. DT MRI tractography showed disconnections in the fronto-parietal regions, concerning principally the superior longitudinal fasciculus (SLF). These results suggest an important role for left SLF disconnection in right-side neglect, which complements analogous evidence for right SLF disconnection in left-side neglect.

Keywords Right neglect · Attention · Disconnection · White matter · Stroke

Introduction

Spatial neglect typically affects left-sided events after right-hemisphere damage, with clinical signs such as a “magnetic attraction” of gaze to right-sided stimuli (Gainotti et al. 1991; Toba et al. 2018a, b) and neglect of left-sided items on visual search (Mark et al. 1988). Patients’ attention tends to be captured by right-sided objects and cannot easily disengage from them (Posner et al. 1984; Rastelli et al. 2008). Contralesional right neglect after left-hemisphere damage is less frequently reported, but different studies describe it to range from 0 to 76% in the left brain-damaged population (Bowen et al. 1999). Beis et al. (2004) showed that, in equivalent right and left brain-damaged subacute patients’ samples, when global performance (i.e., neglect signs on at least one test from the battery used) was considered, neglect was twice more frequent after right brain damage (85%), than after left brain damage (43%). This inconsistency in the reported frequency of right neglect is probably first explained by patients’ selection bias, given that spatial disorders are documented less often in left brain-damaged

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patients who frequently present language impairments and have difficulties in understanding tests instructions (Bowen et al. 1999). Nonetheless, descriptions of right-neglect cases after left-hemisphere stroke sometimes do not report aphasia signs; may result from different patterns of hemisphere dominance (Cambier et al. 1985; Fischer et al. 1991), that is another potential bias in the study of right neglect. The moment of testing with respect to the stroke onset is also an important variable to consider. For instance, neglect tested in the acute stage seems to have similar incidences on right and left brain-damaged patients (62% left neglect and 72% right neglect) (Stone et al. 1991), whereas in the subacute stage contralesional neglect affects only 33% of left-hemisphere stroke patients, but 75% of right brain-damaged patients (Stone et al. 1992). Lastly, the variety of tests used in assessing neglect (Bowen et al. 1999), and the intra-hemispheric lesion localization are also essential issues to consider in quantitative studies comparing right to left neglect.

If quantitatively there is no current agreement concerning right neglect, qualitatively, right-neglect deficits were reported to be transient and less severe, and the spatial asymmetries observed in these patients to be non-significant (Weintraub et al. 1996). An analysis of performances obtained by right-neglect patients in a battery of paper-and-pencil tests for assessing neglect (Beis et al. 2004) showed weak correlations between results in different tests. The same analysis in left-neglect patients' results obtained when tested with a similar battery, showed strong correlations between all the tests (Azouvi et al. 2002). These differences seem to confirm results observed clinically, that right neglect after left brain damage is a less consistent phenomenon than the opposite occurrence. Nonetheless, severe and persistent right neglect was documented to occur in patients with bilateral lesions (Weintraub et al. 1996), as well as in patients with neurodegenerative conditions (Andrade et al. 2010; Bartolomeo et al. 1998).

Until now, only a few studies have been conducted on right-sided neglect after left brain damage. Earlier investigations suggested that right neglect would be associated with more anterior lesions in left hemisphere, whereas left neglect would be the result of more posterior right-hemisphere lesions (Ogden 1985). However, this statement has not been confirmed in later studies (Beis et al. 2004) that concluded that right neglect could also be produced by posterior left lesions. In a voxel-based lesion–symptom mapping (VLSM) study conducted in 121 acute left-brain-damaged stroke patients, Beume et al. (2017) reported patterns of neglect partly mirroring critical regions of the right hemisphere known to be associated with left neglect, including the superior and middle temporal gyri, temporal pole, frontal operculum, and insula. Malherbe et al. (2018) analyzed causal functional contributions of grey and white matter regions in the same cohort of Beume et al. (2017)

and emphasized the contributions of the superior temporal gyrus and inferior parietal lobe in the contralesional attentional bias. These findings have been confirmed in another study trying to disentangle between lesional patterns specific to neglect and extinction in right-brain-damaged patients (Beume et al. 2020). In a more recent VLSM study, Moore et al. (2021) suggested that right and left neglect were not anatomically homologous. In this frame, the study of individual cases of right-neglect patients by using a combined analysis of the grey and white matter could shed light not only on the lesional patterns specific to right neglect after left-hemisphere damage, but also more generally on the distribution of the attentional networks in the two hemispheres. To address these issues, the present study used *in vivo* dissection to reveal patterns of disconnection of white matter bundles in three patients with persistent right neglect.

Methods

Clinical data

Three patients with a left-hemisphere stroke, included in the Centre for Cognitive Anatomy database project (Batrancourt et al. 2002) at the Paris Brain Institute, Pitié Salpêtrière Hospital, were selected for the present study. All subjects gave written consent according to the Declaration of Helsinki. The study was approved by the Ile-de-France I research ethics committee.

The first patient (P1) was an 81-year-old right-handed man, retired engineer (14 years of schooling) with a prior history of completely recovered left occipital ischemic stroke 3 years before, that resulted in a right-side hemianopia. He came to the emergency ward because of sudden difficulties in using his right upper limb. In the emergency ward, the same day, he was confused, presented facial asymmetry, no coordination in his movements, a right-sided motor deficit, apraxia and astereognosia for the right upper limb. In addition to a right homonymous hemianopia resulting from his occipital stroke, he showed clinical signs of aphasia, alexia, agraphia, right-side neglect, a right-sided Babinski sign. He remained in the neurological service for 1 month and then in the rehabilitation unit for 2 months. Neuropsychological examinations were realized at 1 month post-onset and at the end of the rehabilitation period (3 months post-onset). At the end of the rehabilitation period, the patient was well oriented and relatively autonomous in daily life activities, despite a slight motor deficit of the superior right limb and a persistent agraphia. Signs of right neglect were still present.

The second patient (P2) was a 73-year-old right-handed man, retired from work (1 year of schooling). He came to the emergency ward because of the sudden onset of right hemiplegia. Global aphasia was reported at the admission. A

shunt was applied to treat a hydrocephalus. One month later, the patient presented only signs of impaired comprehension, anomia and signs of right-side neglect. He remained in the neurological unit for 1 month and then entered the rehabilitation unit. Neuropsychological examinations were realized at 1 month and 3 months after the stroke. At the end of the rehabilitation period, the patient still presented signs of right-side neglect.

The third patient (P3), a 65-year-old right-handed man, retired instructor (5 years of schooling) came to the emergency ward because of the sudden onset of right hemiplegia, global aphasia, right hemianopia and signs of right-side neglect. He remained in the neurological service for 3 weeks and was then admitted to rehabilitation for 2 months. Neuropsychological examinations were realized at 1 month post-onset and at the end of the rehabilitation period (3 months post-onset). At the end of rehabilitation, he had a predominantly expressive aphasia, with slight comprehension difficulties, and right-neglect signs.

Neuropsychological assessment

Visual neglect was assessed by using the *GEREN* standardized paper-and-pencil battery of tests (Azouvi et al. 2006), including: bells cancelation (Gauthier et al. 1989), line bisection (Schenkenberg et al. 1980), copy of a landscape (Gainotti and Tiacci 1971), text reading tests, overlapping figures test (Gainotti et al. 1991) and the Catherine Bergego scale, devised to assess patients' behavior in everyday life. We also used line (Albert 1973) and letter cancelation (Mesulam 1985) and a different version of the line bisection test (D'Erme et al. 1987). Diagnosis of neglect relied on pathological performance on at least one of the tests (Azouvi et al. 2006).

Neuroimaging data

MRI scans including high-resolution T1-weighted, T2, T2 FLAIR and diffusion-weighted images were obtained for each patient on a 3T GE scanner with a standard head coil for signal reception 3 months after stroke (4 months for P1). High-resolution T1 3D anatomical SPGR (spoiled gradient recalled) images had the following characteristics: RT [repetition time] = 7164 ms; TE [echo time] = 3124 ms; inversion time = 380 ms; flip angle = 15°; coronal orientation perpendicular to the double echo sequence; acquisition matrix = [0, 288, 256, 0]; voxel resolution = 0.5 × 0.5 × 1.2 mm³; slice thickness = 1.2 mm; spaces between slices = 1.2 mm.

Brain lesions were segmented on 3D T1 sequences using MRIcron software (<https://www.nitrc.org/projects/mricron>) and a graphics tablet (WACOM Intuos A6). Images were then normalized to a standard brain template (MNI 152), using Statistical Parametric Mapping 12 running under

Matlab. The percentage of lesion on grey matter regions in the left hemisphere was computed using the AAL template (Tzourio-Mazoyer et al. 2002).

MRI scans also included a diffusion tensor (DT) sequence, performed using echo-planar imaging with the following parameters: RT (repetition time) = 14 s; TE (echo time) = 75.8 ms; flip angle = 90°; acquisition matrix = [128, 0, 0, 128]; percent phase field of view = 100; slice thickness = 3 mm; voxel resolution = 1, 1, 3 mm³; acquisition time = 13 min. Diffusion weighting was performed along 50 independent directions with a *b*-value of 1000 s/mm². The diffusion-weighted data preprocessing was computed using the FSL software (<http://www.fmrib.ox.ac.uk/fsl/>). During the preprocessing, eddy current-induced distortions were removed and motion distortion corrections were computed; then the estimation of the diffusion tensors was calculated. Using standard computational algorithms, fractional anisotropy (FA), was calculated in the native space. FA threshold was set to 0.2 to exclude most of the voxels with high uncertainty and thus reduce the artifactual reconstruction. The critical angle threshold for stopping tracking in case the algorithm encounters a sharp turn in the fibers direction was fixated at 35°. White matter (WM) tractography was performed using the Trackvis software (<http://trackvis.org/dtk>). Regions of interest (ROI) were defined in order to be used as the starting points of the tracking process and were manually drawn on axial slices of FA maps on places considered 'obligatory passages' along each white matter tract (Catani et al. 2005; Catani and Thiebaut de Schotten 2008; Thiebaut de Schotten et al. 2011). A two ROI approach was used for the intermediate and ventral branches of the superior longitudinal fasciculus (SLF II and III), the inferior fronto-occipital fasciculus (IFOF) and inferior longitudinal fasciculus (ILF) in order to visualize and quantify fibers. All ROIs were demarcated on the native space. Resulting tracts were visually inspected to check for aberrant paths.

Results

Neglect assessment

Patients' performances on the neglect battery are reported in Table 1. All the tests were proposed to all the patients, but sometimes patients refused or were unable (given their state of fatigue) to perform all the tests. At the first assessment (1 month post-onset), P1 presented right-neglect signs in visual search (bells cancelation), in landscape drawing task, as well as a leftward deviation in the 200 mm line bisection. At the second evaluation (3 months post-onset), the patient still presented right neglect on line bisection, visual search, as well as in landscape drawing and text reading, but also in a complementary evaluation including the overlapping figures

Table 1 Neuropsychological evaluation of patients

Neuropsychological evaluation	P1 (81-year-old)		P2 (73-year-old)		P3 (65-year-old)	
	1 m post-onset	3 m post-onset	1 m post-onset	3 m post-onset	1 m post-onset	3 m post-onset
Bells cancelation (L/R hits; max 15/15)	14/11*	12/10*	13/8*	15/14#	14/11*	12/11*
Line cancelation (L/R hits; max 30/30)	29/27	29/27	–	–	30/30	29/30
Letter cancelation (L/R hits; max 30/30)	–	24/16*	–	29/25*	–	29/28*
Landscape drawing (R omissions)	1*	0.5*	0.5*	0	1*	0
Reading (L/R hits; max. 61/55)	61/55	61/52*	NA	NA	NA	NA
Line bisection (% deviation)	–	– 12.71%*	+ 1.7%	– 4.7%	+ 0.5%	+ 1.66%
Overlapping figures (L/R hits; max. 5/5)	5/5	4/5*	5/5	5/5	–	5/5
C. Bergego scale (real-life situations)	–	–	–	14/30*	–	–

For line bisection, positive values indicate rightward deviations, and negative values indicate leftward deviation
m, months; y, year; *, pathological performance; #, pathological performance time; –, missing data; NA, not applicable

(one item forgotten to the right). Patient P1 also had right homonymous hemianopia on confrontation.

Patient P2 presented signs of right-side neglect in visual search and landscape drawing at the first assessment (1 month post-onset). When tested at the end of the rehabilitation program (3 months post-onset), this patient still had a pathological performance in visual search. Neglect battery tests did not show any other pathological performance, but this patient had neglect-related difficulties in real-life situation as assessed by his therapist (Catherine Bergego scale).

Patient P3 presented at 1 month post-onset right-neglect signs in visual search and landscape drawing. At the second evaluation (3 months post-onset), this patient still presented pathological performance on visual search tests. Patient P3 had right homonymous hemianopia on confrontation.

Lesion segmentation

Lesional patterns are depicted in Fig. 1 (see Table 2 for description). For patient P1, the MRI scan documented an old ischemic stroke in the inferior left occipital cortex, affecting both the fusiform and lingual gyri, and a recent left hemorrhagic parietal stroke with moderate perilesional edema in the region extending from the postcentral gyrus to the temporo-parietal junction (TPJ). The latter stroke affected the parietal inferior cortex and the white matter lying in its depth, as well as the angular gyrus. There were also signs of leucoaraiosis and cortico-subcortical atrophy.

Patient P2 presented a left parietal hemorrhagic stroke with ventricular inundation as well as right-hemisphere micro-bleeds.

The patient P3 presented an ischemic stroke and atrophy at the level of the left precentral and postcentral gyri. Bilateral lacunae in the caudate heads and in corpus callosum were also observed.

Tractography results

We used DT MRI tractography to dissect in vivo the white matter bundles. Figure 2 and Table 3 present the reconstructed white matter tracts. Reconstructions were made in both hemispheres to compare the FAs for each tract of interest. In the left hemisphere, DT MRI tractography detected disconnections and low FA values in the fronto-parietal networks. On visual inspection, disconnections were also present in the U-shaped fibers linking the superior and inferior frontal gyri. The left IFOF was well represented in all patients, except for patient P1 who had a partial disconnection in its posterior part, lying in the depth of the occipital lobe, where the first stroke had occurred. In P1, there was also evidence of partial damage to the long fibers of the caudal portion of the left ILF, at the level of the lingual gyrus. In the right hemisphere, DTI tractography revealed no disconnection, except for patient P2, who showed low FA values.

Discussion

In the present study, we report detailed behavioral and anatomical findings in three patients with signs of right-side neglect after left-hemisphere strokes. Two of the patients had predominantly left parietal damage; the third had lesions involving the frontal cortex. Despite this heterogeneity in cortical loci of lesions, white matter tractography demonstrated signs of fronto-parietal SLF disconnection in the left hemisphere of all the patients. This finding suggests an important role of left fronto-parietal dysfunction in right-side neglect, and complements analogous evidence for right SLF II-III disconnection in left neglect (Bartolomeo et al. 2012; Bartolomeo et al. 2007; Doricchi et al. 2008; Migliaccio et al. 2012a, b; Migliaccio et al. 2012a, b; Thiebaut de Schotten et al. 2008, 2014, 2005; Toba et al. 2018a, b; Toba et al. 2017; Urbanski et al. 2011).

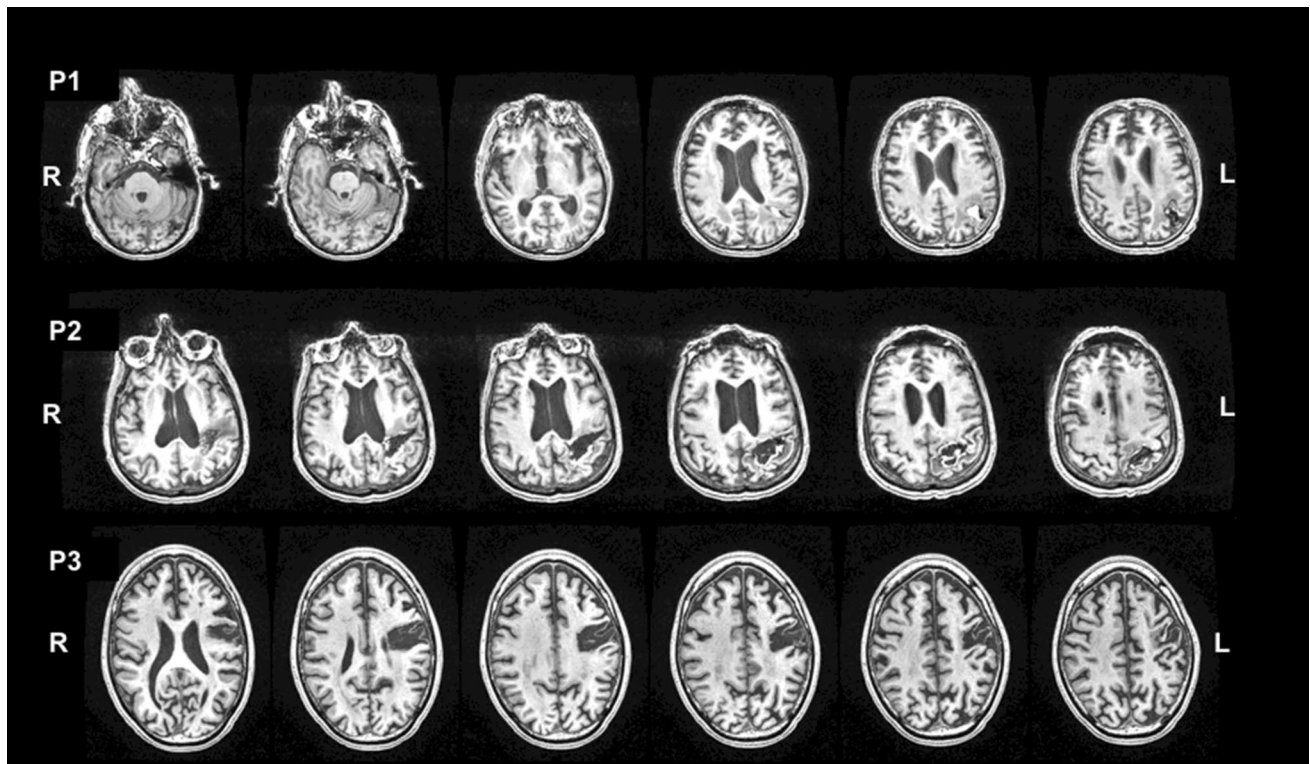


Fig. 1 T1 MRI scans of the three patients in the native space

Table 2 Percentage of lesion on grey matter regions in the left hemisphere (computations were performed with the AAL template, Tzourio-Mazoyer et al. 2002)

Region	% Lesion		
	P1	P2	P3
Precentral	–	10	5.1
Postcentral	0.2	15	29
Supramarginal	3.7	0.5	11
Angular	22.4	–	–
Parietal inferior	18.3	1.4	4.6
Parietal superior	1.4	–	–
Paracentral lobule	–	9.9	–
Cingular middle	–	4.8	–
Lingual	3.8	–	–
Occipital inferior	1.9	–	–
Fusiform	2.6	–	–
Cerebellum_Crus	3.3	–	–
Cerebellum	0.5	–	–

Behavioral results

The three patients analyzed in the study presented with right-neglect signs in paper-and-pencil drawing and visual search tests in the acute stage of the stroke and at 3 months

post-onset. After rehabilitation, results obtained by the patients on the same paper-and-pencil tests only slightly changed. A systematic study assessing neglect in 78 sub-acute left-hemisphere stroke patients (Beis et al. 2004) reported that drawing and visual search tests were the most representative tests to disclose right-side neglect: 12.8% of the tested patients presented with neglect signs on the bells test and 10.4% on landscape drawing. Importantly, these tests were also the most representative for the diagnosis of left-side neglect, as observed by Azouvi et al. (2002). Moreover, in previous studies, the error patterns of patients after left-hemisphere lesions were characterized by: (1) target omissions to both left and right sides of the page; (2) fewer omissions of targets overall, compared with patients with right-hemisphere or bilateral lesions; and (3) non-significant hemispatial asymmetries (Weintraub et al. 1996). Our patients also subscribed to this general right-neglect error pattern, with omissions on both sides of the page in visual search tasks. However, in the landscape copy, two (P2 and P3) out of the three patients achieved correct performance on this task after rehabilitation. Furthermore, one patient (P1) presented with pathological line bisection that persisted also at the second evaluation. Previous studies showed that only 6.4% of left brain-damaged patients had signs of neglect on this task (Beis et al. 2004) and that biased line bisection in long lines (200 mm) was mainly correlated with posterior

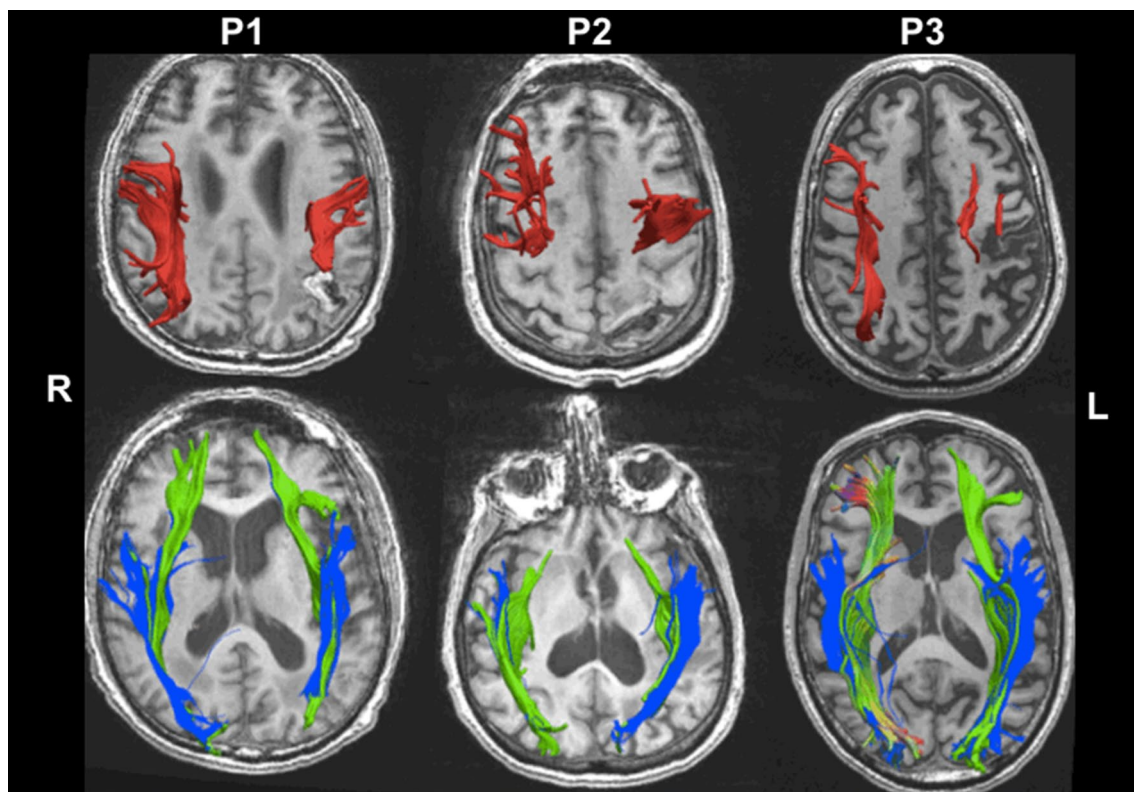


Fig. 2 Reconstructions in native space of the principal tracts of interest in the left (L) hemisphere and in the right (R) hemisphere. Note the loss of fibers in left-hemisphere SLF in all the patients, as well

as the caudal loss of fibers in the IFOF and ILF bundles in P1. Red: superior longitudinal fasciculus; green: inferior fronto-occipital fasciculus; blue: inferior longitudinal fasciculus; R: right; L: left

Table 3 Values of fractional anisotropy (FA) of white matter bundles reconstructed in each hemisphere

Patients	SLF II R	SLF II L	SLF III R	SLF III L	IFOF R	IFOF L	ILF R	ILF L
P1	0.40	0.34	0.43	0.36	0.44	0.46	0.43	0.40
P2	0.35	0.35	0.37	0.35	0.41	0.43	0.40	0.44
P3	0.39	0.33	0.42	0.25	0.47	0.48	0.43	0.44

Note the low FA values of the SLF. Maximum damage was observed in the left SLF

SLF superior longitudinal fasciculus, IFOF inferior fronto-occipital fasciculus, ILF inferior longitudinal fasciculus, L left, R right

lesions (retrorolandic cortex, including parietal, but also temporal or occipital regions, or both). These data are in agreement with the lesion localization of our patient. However, an inconsistent pattern of errors in line bisection should be noted for P1 in the second clinical assessment, where we observed deviations towards either the right or the left in the test version proposed by D'Erme et al. (1987).

In addition, only patient P1 made one right-sided omission in the overlapping figures test in the second evaluation (at 3 months), this test being perfectly completed at the first evaluation (and perfectly completed by the other patients). Performance of right-neglect patients on the overlapping figures test can be variable, being one of the reasons for which right and left neglect are considered as having (at

least in part) different natures and underlying mechanisms (Beis et al. 2004; Gainotti et al. 1986). The overlapping figures were designed to test the focusing of attention on a relatively small display situated in the central vision. This is in contrast with tests requiring the exploration of larger displays, which are more likely to induce right-sided omissions in left brain-damaged patients (Gainotti et al. 1986). In the original study, when neglect was assessed on the basis of the contralateral extrapersonal space exploration, 41% of the right and 37% of the left brain-damaged patients in the explored population had pathological performance. When the capacity to focus attention in central vision (as assessed with the overlapping figures) was tested, a significant difference was observed, with pathological performance in 36%

of the right and only 11% of the left brain-damaged patients from the same population (Gainotti et al. 1986). It remains to be seen whether distinct behavioral components of right-side can be identified, as it is the case for left-side neglect (S  roff et al. 2007). A limitation of the present study is that we only focused on extrapersonal neglect. Future studies should evaluate also signs of personal and motor neglect (Toba et al. 2021) in left-brain-damaged patients.

Anatomical results

Results obtained in this study emphasize the role of left SLF disconnection in right-side neglect in three patients presenting focal parietal and frontal strokes in the left hemisphere. Abnormalities affected both the SLF II and SLF III branches. Early studies on right neglect suggested that it would be preferentially associated with anterior lesions (Ogden, 1985). Beis et al. (2004) found evidence against this hypothesis, because in their sample pathological performance in line bisection, gaze deviation, anosognosia for visual and motor impairment and personal neglect correlated with left posterior lesions (retrorolandic cortex, including parietal, temporal and occipital regions). A control group including patients with left SLF disconnection (affecting SLF II and SLF III branches separately or simultaneously) but without right-neglect symptoms could allow to better characterize the role of this bundle in the left hemisphere. This was not possible in the present study, because candidate patients with left SLF damage also had severe language deficits, which precluded their participation. Other studies considered the possibility that right neglect would be the result of lesions situated in one or more left-hemisphere regions, analogous to those areas producing neglect in the right hemisphere and constituting parts of a proposed neuroanatomical network for the spatial distribution of attention (posterior parietal cortex, frontal eye field, cingulate areas, thalamus, caudate, as well as their interconnections) (Mesulam 1981, 1990). Our results agree with previous studies in confirming this hypothesis (Beume et al. 2017; Beume et al. 2020; Malherbe et al. 2018, see, however, Moore et al. 2021). Generally, severe right neglect was documented to be present in patients with bilateral lesions situated in parietal, occipital and temporal regions, but also in the basal ganglia and the thalamus, the larger of the two lesions being situated in the left hemisphere, posterior to the central sulcus (Bartolomeo et al. 1998; Weintraub et al. 1996). Among the three patients studied here, P2 had low FA values of the SLF in both hemispheres, suggesting possible dysfunction of the right-hemisphere SLF networks. Patient P3 presented lacunes in the corpus callosum with a possible impact on the transfer of the information relevant for visuospatial attention among the two hemispheres. Inter-hemispheric disconnection, which may play a role in the chronic persistence of left neglect

(Bartolomeo 2019, 2021; Lunven et al. 2019, 2015), might also contribute to lack of compensation from the healthy hemisphere (Bartolomeo and Thiebaut de Schotten 2016) in cases of right-sided neglect. Patient P1 presented cortico-subcortical atrophy in both hemispheres, which may also suggest concomitant right-hemisphere dysfunction. In the present study, the characteristics of DTI data made it impossible to directly study the FA of commissural fibers, particularly those linking temporo-parietal, parietal and frontal areas of both hemispheres. Further data are needed in order to confirm the hypothesis of the necessity of bilateral lesions in severe right neglect, and to specify the role of intra- and inter-hemispheric plasticity in neglect compensation (Charras et al. 2015; Stengel et al. 2022; Toba and Barbeau 2021).

Implication for attentional models

Given that left neglect is more frequent, persistent and severe than right neglect after unilateral lesions, several theories attributed a dominant role to the right hemisphere for the control of spatial distribution of attention (Heilman et al. 1993; Mesulam, 1999). These models postulate that the right hemisphere directs attention to both ipsilateral and contralateral hemispaces, whereas the left hemisphere is shifting attention only to the right hemispace. Thus, a single lesion in the right hemisphere gives rise to severe neglect because the intact left hemisphere does not have a role in the symmetrical deployment of attention, but only in directing attention to the right. A left-hemisphere lesion could produce right neglect, but this would be compensated by the symmetrical distribution of attention controlled by the right hemisphere. Later, Corbetta and Shulman (2002) described: (1) an attentional ventral system largely lateralized in the right hemisphere, specialized in the detection of behaviorally relevant stimuli, and (2) an attentional dorsal system distributed bilaterally, and involved in preparing and applying goal-directed behavior. The two systems are in permanent interaction in normal brains and both would be disturbed in neglect. That is, in these distributed large-scale networks, the left-hemisphere correct functioning would also be essential in the deployment of spatial attention. This assumption has also been proposed in one of the earliest models of spatial attention (Kinsbourne 1977), and confirmed in a later study conducted on left-neglect patients (Corbetta et al. 2005), which used fMRI to disclose abnormal activations in structurally intact left-hemisphere areas. Thus, the rightward spatial bias of acute neglect patients was associated with hyperactivity in the left dorsal parietal cortex, which normalized in the chronic stage and was accompanied by the behavioral recovery. Support to this model of hemispheric imbalance also came from a study (Vuilleumier et al. 1996) that reported recovery of spatial neglect (resulting from a right-hemisphere stroke) after a second

stroke in the left hemisphere (see also Toba et al. 2020a, b, c; Valero-Cabré et al. 2020 and Stengel et al. 2022 for reviews). Inspired by these results, studies using non-invasive brain stimulation aimed at normalizing the imbalance between the activity of the two hemispheres after stroke (see Cazzoli et al. 2012; Koch et al. 2012, 2008; Nyffeler et al. 2019). The patients presenting neglect after left-hemisphere lesions presented in the current study suggest, based on an *in vivo* reconstruction of white matter bundles, in agreement with functional MRI studies (Corbetta et al. 2005), that also the left hemisphere has an important role in the distribution of spatial attention. Alternatively, or in addition, some degree of dysfunction in the right-hemisphere SLF III network might be necessary for signs of right-side neglect to emerge (Bartolomeo and Seidel Malkinson 2019). Such a possibility implicates that both hemispheres should be lesioned for chronic right-neglect signs to occur. Moreover, some degree of inter-individual variability in visuospatial competence of the left hemisphere (and particularly of the left SLF networks) could be responsible of the low rate of occurrence of neglect after left-hemisphere stroke. As observed in language (Knecht et al. 2002), healthy human subjects might differ in lateralization of visuospatial attention-related brain activation; if so, then the presence of neglect might correlate with the degree and side of lateralization of visuospatial attention networks. This hypothesis could pave the way for future directions in visuospatial attention studies.

Conclusion

In vivo white matter dissection in three patients with right-sided neglect suggests a role for left fronto-parietal network disconnection in neglect signs, and complements analogous evidence for right SLF disconnection in left neglect.

Acknowledgements We are thankful to Dr B. Batrancourt for managing the Centre for Cognitive Anatomy database project. We thank the Naturalia & Biologia Foundation for providing travel grants for some of the co-authors.

Author contributions All the authors contributed to the study conception and design. Material preparation and data collection were performed by MNT. Analyses were performed by MNT and RM. The first draft of the manuscript was written by MNT, and all the authors commented on previous versions of the manuscript. All the authors read and approved the final manuscript.

Funding The work of Dr Bartolomeo is supported by Agence Nationale de la Recherche through ANR-16-CE37-0005 and ANR-10-IAIHU-06.

Data availability Data will be made available on reasonable request.

Declarations

Conflict of interest The authors declare they have no relevant financial or non-financial interests to disclose.

Ethical approval All the subjects gave written consent according to the Declaration of Helsinki. The study was approved by the Ile-de-France I research ethics committee.

Consent to participate Patients consented to participate in the Centre for Cognitive Anatomy database project at the Paris Brain Institute, Pitié Salpêtrière Hospital.

Consent to publish Participants provided informed consent in the Centre for Cognitive Anatomy database project.

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