

Different patterns of confabulation in left visuo-spatial neglect

Gianfranco Dalla Barba, Marta Brazzarola, Claudia Barbera, Sara Marangoni, Francesco Causin, Paolo Bartolomeo, Michel Thiebaut de Schotten

▶ To cite this version:

Gianfranco Dalla Barba, Marta Brazzarola, Claudia Barbera, Sara Marangoni, Francesco Causin, et al.. Different patterns of confabulation in left visuo-spatial neglect. Experimental Brain Research, 2018, 236 (7), pp.2037 - 2046. 10.1007/s00221-018-5281-8. hal-01845516

HAL Id: hal-01845516 https://hal.sorbonne-universite.fr/hal-01845516

Submitted on 20 Jul 2018

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers. L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Different patterns of confabulation in left visuo-spatial neglect

Gianfranco Dalla Barba^{1, 2, 3,4}, Marta Brazzarola⁴, Claudia Barbera⁴, Sara Marangoni⁴, Francesco Causin⁵, Paolo Bartolomeo^{6*}, Michel Thiebaut de Schotten^{6-8*}

¹INSERM, Paris, France

²Institut de la Mémoire et de la Maladie d'Alzheimer (IM2A), Département de Neurologie, Hôpital de la Pitié-Salpêtrière, Sorbonne Université, Paris, France

³Dipartimento di Scienze della Vita, Università degli Studi di Trieste, Italy

⁴Centro Medico di Foniatria, Unità Operativa Complessa di Riabilitazione Neurocognitiva, Padova, Italy

⁵Azienda Ospedaliera di Padova, Unità Operativa Complessa di Neuroradiologia, Padova, Italy

⁶INSERM U 1127, CNRS UMR 7225, Sorbonne Université, Institut du Cerveau et de la Moelle épinière (ICM), F-75013 Paris, France.

⁷Brain Connectivity Behaviour group, Sorbonne Universities, Paris, France

⁸Groupe d'Imagerie Neurofonctionnelle, Institut des Maladies Neurodégénératives - UMR 5293, CNRS, CEA University of Bordeaux, Bordeaux, France

*Contributed equally

keywords: confabulation, neglect, implicit knowledge

Corresponding author: Paolo Bartolomeo

INSTITUT DU CERVEAU ET DE LA MOELLE EPINIERE

HOPITAL PITIE-SALPETRIERE

47 BOULEVARD DE L'HOPITAL

CS 21414

75646 PARIS CEDEX 13

email: paolo.bartolomeo@gmail.com

tel: +33157274140

ABSTRACT

Confabulating patients produce statements and actions that are unintentionally incongruous to their history, background, present and future situation. Here we present the very unusual case of a patient with right hemisphere damage and signs of left visual neglect, who, when presented with visual stimuli, confabulated both for consciously undetected and for consciously detected left-sided details. Advanced anatomical investigation suggested a disconnection between the parietal and the temporal lobes in the right hemisphere. A disconnection between the ventral cortical visual stream and the dorsal fronto-parietal networks in the right hemisphere may contribute to confabulatory behaviour by restricting processing of left-sided stimuli to pre-conscious stages in the ventral visual stream.

1. INTRODUCTION

Confabulation is a rather infrequent disorder, which consists in the production of actions and verbal statements incongruous to the subject's history, background, present and future situation (Dalla Barba, 1993). It has been described in several pathological conditions, including visual neglect. Patients with visual neglect may confabulate on the neglected stimuli, however, only few studies reported this phenomenon (e.g. Chatterjee, 1995; Manning & Kartsounis, 1993). Clinically, patients with visuo-spatial neglect may show signs of so-called 'implicit' or partial knowledge of otherwise unreported stimuli presented in the neglected field (Bartolomeo, 2014; Marshall & Halligan, 1988). This partial knowledge is sometimes inaccurate and fits within the standard definition of a confabulation. This suggests that visual information may have been partially processed in the brain but did not access consciousness for these patients. Pre-conscious, pre-attentional processing of the neglected stimuli, would be similar to that of patients with 'blindsight' (Weiskrantz, 1987) and prosopagnosia (De Haan, Young, & Newcombe, 1991) but its anatomical mechanism remains largely unknown.

Drawing on a suggestion by Geschwind (1965), Bartolomeo et al. (2007) proposed that confabulations for neglected items could result from poor transfer of right hemisphere-based, knowledge of left-sided visual stimuli to the left hemisphere. Hence, the verbalisation of the residual visual information by the left hemisphere would be at the basis of confabulatory responses.

Alternatively or in addition, intra-hemispheric disconnection may restrict processing of left-sided stimuli to a pre-conscious stage of processing. To access consciousness, sensory contents must compete, before one of them becomes dominant and accesses the limited capacity of our consciousness (i.e. Global Workspace theory, Baars, 1988). Information is pre-processed, at first preconsciously, within modular cerebral networks such as, for instance,

those contained in the visual cortical ventral stream (Ungerleider & Mishkin, 1982). Attentional amplification through fronto-parietal networks can then bring information to a conscious level of processing, and make it available to verbal report. A disconnection between the visual ventral stream and fronto-parietal network might therefore lead to 'implicit' or partial knowledge of stimuli presented in the neglected field. Support for this hypothesis comes from neuroimaging studies demonstrating preserved sensory activation to undetected stimuli in brain-damaged patients (Rees, et al., 2000; Vuilleumier, et al., 2001). In the present context, this hypothesis would predict that the patient's verbal report would again be based on inadequate processing of information, and liable to be confabulatory (Bartolomeo, de Vito, & Seidel Malkinson, 2016). For instance, when confronted with the well-known images of two identical houses, except for flames coming from the left part of one of them, and asked which house he would like to live in (Marshall and Halligan, 1988), the patient reported by Manning and Kartsounis (1993) chose the non-burning house and confabulated that it had an extra fireplace. Another patient described by Bisiach and Rusconi (1990) paradoxically kept choosing the "burning" house, considering it more "spacious" on the burning side, where the contour of the flames actually enlarged the shape of the house. In a group of 13 neglect patients Doricchi et al. (1997) described different patterns of responses motivating correct implicit choices of the "non-burning house": 1) "there is no specific reason for my choice, the two houses are the same anyway," suggesting complete uncoupling of verbal output from implicit processing; 2) "the house I chose is 'better', 'bigger', or 'works better',' suggesting, in this case, some approximation of verbal output to implicit processing.

In this paper we describe the very unusual case of a patient with left visuo-spatial neglect, who confabulated both for consciously undetected and for consciously detected stimuli presented in the neglected field. Advanced neuroimaging methods, including tractography

were employed to test inter- and intra-hemispheric disconnection hypotheses accounting for confabulatory behaviour.

2. CASE REPORT

2.1. History

PC is a 70-years-old right-handed businessman with thirteen years of education. He is married and has two children. He has no history of psychiatric or previous neurologic diseases.

In October 2014 he was admitted to the Internal Medicine Department of the Padua University Hospital for sudden loss of consciousness. A CT brain-scan showed a right temporo-parietal ischemic stroke. Due to the appearance of epileptic seizures, he was transferred to an intensive care unit and then to the Neurology Department of the same hospital. Twenty days later he was referred to the Neurocognitive Rehabilitation Unit of the *Centro Medico di Foniatria* in Padua to undergo cognitive rehabilitation.

2.2. Neuropsychological examination.

PC was tested on various occasions between November 2014 and January 2015 (Table 1).

Insert Table 1 about here

The ethical committee of the *Centro Medico di Foniatria* approved the experimental procedures. The patient provided written informed consent for publication of this case report. He was fully cooperative, well oriented in time and place and had preserved general intellectual abilities. Clinically he was not amnesic. He performed normally on learning, episodic memory tests, except for the recall of the Rey's figure. The copy of the Rey's figure

was affected by some omissions both on the right and on the left side, and was not informative about the patient's neglect.

Executive functions, short-term memory and working memory were normal. He performed normally on tests of oral expression, understanding of oral language and praxis. Visual perception, as measured with the VOSP Screening test and Object Decision, was unimpaired. On clinical criteria, PC showed typical signs of left visuo-spatial neglect, both in ecological conditions and in classical tests sensitive to this disorder, such as line crossing, line bisection, shape and letter cancellation. PC was anosognosic for his neglect disorder.

2.3. Experimental investigation.

The following observations were made during five testing sessions, 8 weeks after the stroke. Partially following and expanding the procedure introduced by Marshall and Halligan (1988), PC was presented with drawings of 9 pairs of objects. For each pair, vertically arranged objects were identical, except for a salient detail on the left side. The stimuli were: 1. Two houses, in one of which flames were emerging from the left side of the house; 2. Two banknotes, in one of which the left part was missing; 3. Two vases, an empty one and one with a flower on the left side; 4. Two trees, in one of which the left part was missing; 5. Two wine glasses, one of which was broken in the left side; 6. Two Eiffel Towers, in one of which the left part was missing; 7. Two cows, in one of which the left part was missing; 8. Two ambulances, in one of which a left-sided wheel was missing; 9 Two sailing boats, one of which had a leak on the left side.

2.3.1. Procedure

The 9 stimuli were presented (Fig. 1) to PC in 5 sessions, one session per day for 5 consecutive days. In each session, the two houses were presented to the patient 12 times with alternate vertical order (in each session six times the burning house was above the other house). The other stimuli were presented one time per session. In our testing set there were

more burning houses than other stimuli, because this type of stimulus provided significant results in the Marshall and Halligan's seminal study (Marshall & Halligan, 1988). The rationale for including more "burning houses" than other stimuli was to confirm, support and reproduce the Marshall & Halligan results and to see whether these results could be extended to other stimuli.

Insert Figure 1 about here

For the houses, the examiner asked PC if they were "the same or different". After each presentation, the examiner asked the patient to say which house he would prefer to live in and why. For each of the other stimuli, the examiner asked PC if the two items were "the same or different", then which of the two he would chose and why.

The same stimuli were presented with the same procedure to 10 age- and education-matched normal controls (NC).

2.3.2. Results

In the statistical analyses the α value was set at 0.05. The Crawford et al's method for statistical analysis of single case (Crawford, Garthwaite, & Wood, 2010) was used where possible. The Chi Square test was used in other cases.

All the normal controls were able to identify the differences between the items for each display, and to name them correctly. They were all able to tell what the difference between the two stimuli was (e.g., by mentioning the flames in the burning house), and to choose which item they would prefer (e.g. an intact boat rather than a boat with a leak).

On the other hand, the patient, when presented with the houses, never noticed the presence of flames for any of the 60 trials (12 x 5 sessions), but responded that the houses were

different and always chose to live in the house *with* flames. On some occasions the examiner, pointing at the flames, asked PC: "Could this be fire?" "No, it can't be fire, replied PC. Fire goes up." "But it does go up", insisted the examiner. "No, continued PC, it should come out from the above window and from the fireplace" (there was no above window). When the examiner asked why he would prefer to live in the burning house, in 50/60 trials PC confabulated giving one of the following answers: "Because there is a pergola" (18 times), "Because there are grapes" (11 times), "Because there is a little plant" (8 times), "Because it is more linear" (6 times), "Because it is cleaner" (5 times), "Because in this house they cook better food" (1 time), "Because it is more real" (1 time). In the remaining 10/60 trials PC did not provide any reason for his choice, stating that he did not know why he preferred the burning house. The difference with NC's responses was statistically significant (*p*< .05).

Concerning the other stimuli, PC's performance varied. For the banknotes he always said that they were the same, but always chose the entire one, saying once "Because it is more beautiful", and "I don't know" in the remaining trials. For the cows four times he said that the two items were the same, always choosing the entire one, saying, "Because it is a cow", "Because is more real", "Because it has a different profile", "Because it has a straight back". For the remaining 6 stimuli he always said that they were different, and always chose the entire item, "Because it is complete".

2.4. Examination of confabulation

PC showed confabulatory behaviour outside the experimental context, mainly in informal conversation.

Since PC showed a marked tendency to confabulate in the experiment described in the previous section, it was decided to evaluate whether he would confabulate in other domains and in particular in the various memory domains, where confabulation is classically described. Accordingly, PC was administered the Confabulation Battery (CB). The CB

involves the retrieval of various kinds of information and consist of 165 questions, 15 for each of the 11 following domains: (1) Personal Semantic Memory, (2) Episodic Memory, (3) Orientation in time and place, (4) Linguistic Semantic Memory, General Semantic Memory (5) Recent, (6) Contemporary, (7) Historical, (8) Semantic Plans, (9) Episodic Plans and questions to which the appropriate response would be 'I don't know', both (10) semantic and (11) episodic. Each domain has been described in detail elsewhere (Dalla Barba & Decaix, 2009).

2.4.1. Procedure

Questions from the 11 domains were randomized and presented to the patient and to 10 age- and education-matched normal controls (NC). Responses were scored as "correct, "wrong", "I don't know" and "confabulation". For episodic memory, responses were scored "correct" when they matched information obtained from the patient's relatives. Correct responses were self-evident for semantic memory questions. For "I don't know" questions, both Semantic and Episodic, a "I don't know" response was scored as correct. Because there is no sufficiently acceptable external criterion capable of defining confabulation, for its detection an arbitrary decision necessarily had to be made.

To distinguish between a wrong response and a confabulation, a clear-cut decision was adopted only for answers to questions probing orientation in time. In this case the strictest criterion was chosen: answers to questions regarding the current year, season, month, day of the month, day of the week, and hour of the day were judged to be confabulations only if erring for more than 5 years, 1 season, 2 months, 10 days, 3 days or 4 hours, respectively. Answers to the other questions of the Confabulation Battery were independently rated as "correct", "wrong" and "confabulation" by four different raters, with 100% interrater reliability. It must be emphasised that the decision as to whether an answer was wrong or confabulatory was never puzzling, although it may have been made on an arbitrary of

subjective basis. As far as questions concerning personal and semantic plans are concerned, it might be argued that any possible answer is a confabulation, since, by definition, the future is only "probable" and there is in principle no "correct" answer to questions about the future. Yet, answers about the future can be definitely confabulatory when they show a marked discrepancy or a real contradiction with what a predicted future event might be, in view of the present situation. For example, although he was hospitalised, to the question "When will you take vacations, or when will you be travelling next time?", PC answered "Next Tuesday."

2.4.2. *Results*

PC's correct responses and confabulations are reported on Table 2.

Insert Table 2 about here

PC produced significantly fewer correct responses than NC, who performed at ceiling, to Episodic Memory, Orientation in Time and Place, Episodic Plans, "I don't know" Semantic and "I don't know" Episodic questions (all p < .05), and confabulated significantly more than NC answering Episodic Memory and "I don't know" Semantic and Episodic questions (all p < .05), questions which are known to elicit confabulation much more than standard episodic memory tests.

According to the criteria proposed elsewhere (Serra, et al., 2014), PC was a severe confabulator since he produced 40% or more of confabulations in Episodic Memory. Confabulations were also prominent in "I don't know" Episodic and in "I don't know" Semantic questions, whereas they were absent or sporadic in other domains of the CB. Following the taxonomy of confabulation proposed by the Dalla Barba's group (Dalla Barba & Boisse, 2010; La Corte, Serra, Attali, Boisse, & Dalla Barba, 2010), 68% of PC's

confabulations were "Habits Confabulations,", i.e. either repeated personal events mistaken as specific, unique past and future personal episodes, or public events when semantic knowledge is concerned. This confirms previous results showing that this type of confabulations is the most frequently observed (Dalla Barba & Boisse, 2010; La Corte, et al., 2010). Other types of confabulation were: 16% Memory Confusions, 4% Memory Fabrications, 12% Misplacements.

2.5. Anatomical study

2.5.1 Acquisition parameters

We acquired diffusion-weighted imaging (DWI) which provided isotropic (2 × 2 × 2 mm) resolution and coverage of the whole head with a posterior-anterior phase of acquisition. A total of 65 near-axial slices were acquired on a Philips Ingenia 3T system equipped with a 32-channel head coil. We used an echo time (TE) of [96"] msec and a repetition time (TR) of [10104"] msec. At each slice location, 1 image was acquired with no diffusion gradient applied (i.e. B0). Additionally, 32 diffusion-weighted images were acquired, in which gradient directions were uniformly distributed on the hemisphere with electrostatic repulsion. The diffusion weighting was equal to a b-value of 1000 sec mm⁻². Finally, at each slice, diffusion-weighted data were simultaneously registered and corrected for subject motion and geometrical distortion adjusting the gradient accordingly (http://www.exploredti.com; see (Leemans & Jones, 2009).

2.5.1 Atlas-Based Analysis of Disconnection

The patient's lesion was first drawn on the native B0 image using MRIcron (http://http://www.cabiatl.com/mricron) by an expert anatomist (M.T.S.) (Fig. 2a). B0 image was then normalized to a standard brain template, (MNI152, Montreal Neurological Institute link) using rigid (FLIRT) and elastic (FNIRT) deformation tools provided FSL. We calculated and applied the deformations to the whole brain except the lesion mask to avoid deformation of the lesioned tissue (Brett, Leff, Rorden, & Ashburner, 2001; Volle, et al., 2008). The

deformation was subsequently applied to the original drawing of the lesion as illustrated in Fig. 2b. We mapped the normalized lesion onto tractography reconstructions of white matter pathways obtained from a group of healthy controls (Rojkova, et al., 2015). We used 50% overlap maps for the localization and quantification of the lesions (Thiebaut de Schotten, et al., 2015; Thiebaut de Schotten, et al., 2014). We quantified the severity of the disconnection by measuring the proportion of the tract to be disconnected (Thiebaut de Schotten, et al., 2015) using Tractotron software as part of the BCBtoolkit (http://toolkit.bcblab.com). Results displayed in Fig 2c indicated that, when compared to control brains, the lesion damaged 19% of the long and 13% of the posterior segments of the arcuate fasciculus, 16% of the optic radiations and 11% of the inferior longitudinal fasciculus. The lesion damaged less than 5% of all other tracts.

2.5.2 Lesion-Based Approach to Mapping Disconnection

We further capitalized on recently published methods to reveal brain areas deafferented by the lesion using a disconnectome map approach (Foulon, et al., 2018).

The patient's lesion was registered to the tractography of a group of healthy controls (Rojkova et al., 2015) using affine and diffeomorphic deformations (Klein et al., 2009; Avants et al., 2011). The registered lesion was subsequently used as a seed point to track streamlines in an healthy dataset using Disconnectome maps software as part of the BCBtoolkit (http://toolkit.bcblab.com) (Foulon, et al., 2018). Subsequently, we created a binary visitation map of the streamlines intersecting the lesion. This map was normalized to MNI space using the inverse of the affine and diffeomorphic deformations mentioned above. Percentage maps were computed by summing at each voxel in the MNI space the normalized visitation map of each subject and projected onto the average 3D rendering of MNI152 using anatomist (http://brainvisa.info). Fig. 2d indicates a high probability of deafferentation of the posterior part of the temporal lobe and the inferior parietal lobule.

2.5.3 Tractography

We used tractography of diffusion-weighted imaging to confirm the disconnection identified by tractotron (i.e. damage to the long and of the posterior segments of the arcuate fasciculus, the optic radiations as well as the inferior longitudinal fasciculus).

A damped Richardson Lucy Spherical Deconvolution (Dell'Acqua, et al., 2010) was computed to estimate multiple orientations in voxels containing different populations of crossing fibres (Alexander, 2006; Anderson, 2005; Tournier, Calamante, Gadian, & Connelly, 2004).

Algorithm parameters were chosen as previously described (Dell'Acqua, Simmons, Williams, & Catani, 2013). A fixed-fibre response corresponding to a shape factor of $\alpha = 2 \times 10-3$ mm2/s was chosen (Dell'Acqua, et al., 2013).

Whole brain tractography was performed selecting every brain voxel with at least one fibre orientation as a seed voxel. From these voxels, and for each fibre orientation, streamlines were propagated using Euler integration with a step size of 1 mm (as described in Dell'Acqua, et al., 2013). When entering a region with crossing white matter bundles, the algorithm followed the orientation vector of least curvature (as described in Schmahmann & Pandya, 2007). Streamlines were halted when a voxel without fibre orientation was reached or when the curvature between two steps exceeded a threshold of 45°. Spherical deconvolution, fibre orientation vector estimations and tractography were performed using in Startrack (http://www.natbrainlab.co.uk).

We explored the integrity of the visual afferent system in the left and the right hemispheres using regions of interest drawn on a coronal section situated at the level of the occipital notch (Fig. 2e).

We further explored the perisylvian network in the left and the right hemispheres using regions of interest drawn on axial sections including voxels concerned by associative perisylvian white matter as reported in Catani et al. (Catani, Jones, & ffytche, 2005) (Fig. 2f).

Unfortunately, the available 30 directions were not sufficient to reconstruct the dorsal fronto-parietal network as previously reported in (Thiebaut de Schotten, et al., 2011)

Results presented in Fig. 2e and 2f solely display tracks passing by the defined regions of interest and revealed a clear-cut disconnection of the posterior and long segments of the arcuate fasciculus in the right hemisphere, partial damage of the optic radiations with a relative sparing of the inferior longitudinal fasciculus, as well as of interhemispheric connections.

3. DISCUSSION

We reported an extensive behavioural and anatomical study of PC, a patient with right hemisphere damage, who, at the time of testing, suffered from relatively pure left neglect, in the sense that his visuo-spatial abilities were affected out of all proportion to other cognitive functions and he was otherwise alert and responsive. In particular, he was not demented, had normal visual perception and performed normally on tasks of executive functions, short-term memory, working memory, episodic memory, semantic memory and praxis. Importantly, PC showed a severe (Serra, et al., 2014) tendency to confabulate on the Confabulation Battery, a sensitive tool to detect confabulations in various memory domains.

When presented with visual items differing on their left side, PC showed three patterns of performance: 1. He gave "normal" responses (30 times), i.e. he detected the difference between the two items of the stimulus and chose the entire one. 2. He didn't detect the difference between the two items of the stimulus (9 times), made a "normal" choice of the

"better" one, and confabulated on the reason of his choice (5 times) 3. He detected a difference between the two items of the burning house task (without identifying the flames as such), then chose the unexpected one (the burning house), and confabulated on the reason of his choice (49 times).

Confabulation is often considered a memory distortion associated to a frontal lobe lesion. However, it has been shown that confabulation is not associated to a specific brain lesion (Dalla Barba, Brazzarola, Marangoni, Barbera, & Zannoni, 2017; Dalla Barba & La Corte, 2013, 2015), but can occur in patients with lesions in more than twenty anterior and posterior brain regions.

PC was not amnesic either clinically, or in formal testing and performed normally in frontal tests. The results of the present study add evidence that confabulation may occur outside memory deficits (Papagno & Baddeley, 1997), and that a frontal lesion is not necessary for patients to confabulate (Dalla Barba, Boissé, Bartolomeo, & Bachoud-Lévi, 1997).

As far as "normal" responses are concerned, as compared to other types of responses, these can be the result of fluctuations of PC's performance. It is well known that brain damaged patients rarely show a clear-cut performance. Notwithstanding the cognitive domain involved, patients with brain damage show, in variable proportion, both correct and incorrect responses when challenged in testing or in experimental situations. This pattern of performance is often observed in neglect patients, likely because of fluctuations in their level of alertness (Bartolomeo, 2014). Therefore PC's 30% of "normal" responses over the total number of responses is not surprising.

Ten per cent of PC's responses reflected the classical pattern described by Marshall & Halligan (1988): the patient claimed that the two items were identical, yet he chose the 'good' one and confabulated on the reason of his choice. These results are similar to those obtained

in patients with 'blindsight' (Weiskrantz, 1987) and prosopagnosia (De Haan, et al., 1991) and have been interpreted as reflecting pre-attentional, pre-conscious processing (Manning & Kartsounis, 1993; Marshall & Halligan, 1988)

However, the main result of this study is the type of responses PC gave to the "burning house" stimuli. In 60/60 presentations, PC acknowledged a difference between the two houses. However, he never noticed, and actually denied, that one of them was in flame. Although the stimuli were drawn in black and white, none of our control subjects had any doubts about the identity of the flames emerging from the left side of the burning house. When asked which house he would prefer to live in, he always chose the burning house and confabulated about his choice. To the best of our knowledge, such a pattern was only briefly hinted about by Bisiach and Rusconi (1990) in one of their patients. This rare occurrence cannot be accounted for in terms of the classical blindsight-like, pre-conscious, pre-attentional processing interpretation. According to the criteria proposed by the Dalla Barba's group, PC was a severe confabulator, as determined by his responses to the Episodic Memory questions of the CB. However, this doesn't explain PC's perceptual confabulations. PC's general tendency to confabulate may have played a role in his pattern of performance, but it is unlikely to be the key factor. The type of tasks we have proposed in this study have never been proposed to patients with amnesic-confabulatory syndromes, but these patients typically don't confabulate when describing perceptually presented stimuli.

Deficits of spatial working memory may contribute to neglect signs (Malhotra, et al., 2005; Wansard, et al., 2015; Wansard, et al., 2014), albeit with different weights in different patients (Toba, et al., 2018). However, by definition such deficits should affect items that must be remembered, because they are not directly present in the patient's view. This was not the case for the present stimuli, which could be explored at will until response and thus did not require the use of spatial working memory.

Although the pattern of brain lesions in a single patient requires confirmation to be accepted as strong evidence (Bartolomeo, Seidel Malkinson, & de Vito, 2017), the building of a large database of such rare occurrences as confabulations in neglect would be hard to attain in a reasonable time span, and difficult to couple with an extended behavioural study when many patients have to be tested. Also, the excellent level of detail of anatomical study, which is now possible thanks to cutting-edge neuroimaging techniques, is difficult to obtain in large groups. Moreover, anatomical information from single cases can guide the building of testable hypotheses for future research. With these considerations in mind, we now outline possible conclusions about the relationships between PC's pattern of brain damage and his test performance. As suggested in the Introduction, two distinct patterns of white matter disconnection could be at the basis of PC's pattern of performance:

In the case of the "burning house", the right hemisphere might have correctly detected the difference between the two houses. If the left hemisphere is disconnected from the right hemisphere by a posterior callosal lesion, it would not be able to access information processed by the right hemisphere and leading to the production of confabulatory responses (Bartolomeo, et al., 2007; Geschwind, 1965). A similar observation and account was provided by classical studies from Gazzaniga and his group on callosotomized patients (Gazzaniga, 2000).

Alternatively, if the attentional networks were disconnected from the ventral visual stream within the right hemisphere, then left-sided items might not be able to be processed at a conscious level because of lack of attentional amplification. The resulting preconscious visual processing could have primed PC's choices. The patient might subsequently have produced rich confabulatory responses to explain his behaviour.

PC's anatomical investigation supported our second hypothesis, because it revealed an intra-hemispheric temporo-parietal disconnection between occipito-temporal visual

processing conveyed along the inferior longitudinal fasciculus and the fronto-parietal attentional networks. Hence, it is possible that preconscious visual processing of the burning house would have been conveyed along PC's inferior longitudinal fasciculus, but could not reach attentive/conscious processing due to a disconnection of the temporo-parietal segment of the arcuate fasciculus.

In conclusion, we described the rare case of a neglect patient showing confabulation for correctly identified stimuli in the neglected field, in addition to the more frequently described confabulations for undetected stimuli in the neglected field. We propose an intra-hemispheric disconnection account for these observations, stressing disconnection between the parietal and the temporal lobes of the right hemisphere. Future research is needed to assess the frequency of confabulations in neglect patients and their neural correlates.

ACKNOWLEDGEMENTS

The authors declare no conflict of interest. The research leading to these results received funding from the 'Agence Nationale de la Recherche' [grants number ANR-09-EMER-006 and number ANR-13-JSV4-0001-01]. Additional support comes from the program "Investissements d'avenir" ANR-10-IAIHU-06.

REFERENCES

- Alexander, D. C. (2006). An introduction to computational diffusion MRI: the diffusion tensor and beyond. In *Visualization and Processing of Tensor Fields* (pp. 83-106). Berlin: Springer.
- Anderson, A. W. (2005). Measurement of fiber orientation distributions using high angular resolution diffusion imaging. Magnetic resonance in medicine: official journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine, 54, 1194-1206.
- Baars, B. J. (1988). *A Cognitive Theory of Consciousness*: Cambridge University Press Bartolomeo, P. (2014). *Attention disorders after right brain damage*. London: Springer Verlag.
- Bartolomeo, P., Seidel Malkinson, T., & de Vito, S. (2017). Botallo's error, or the quandaries of the universality assumption. Cortex, 86, 176-185.
- Bartolomeo, P., Thiebaut de Schotten, M., & Doricchi, F. (2007). Left unilateral neglect as a disconnection syndrome. Cereb Cortex, 17, 2479-2490.
- Bisiach, E., & Rusconi, M. L. (1990). Break-down of perceptual awareness in unilateral neglect. Cortex, 26, 643-649.
- Brett, M., Leff, A. P., Rorden, C., & Ashburner, J. (2001). Spatial normalization of brain images with focal lesions using cost function masking. Neuroimage, 14, 486-500.
- Catani, M., Jones, D. K., & ffytche, D. H. (2005). Perisylvian language networks of the human brain. Annals of Neurolology, 57, 8-16.
- Chatterjee, A. (1995). Cross-over, completion and confabulation in unilateral spatial neglect. Brain, 118 (Pt 2), 455-465.
- Crawford, J. R., Garthwaite, P. H., & Wood, L. T. (2010). Inferential methods for comparing two single cases. Cognitive neuropsychology, 27, 377-400.
- Dalla Barba, G. (1993). Confabulation: Knowledge and recollective experience. Cognitive Neuropsychology, 10, 1-20.
- Dalla Barba, G., & Boisse, M. F. (2010). Temporal consciousness and confabulation: is the medial temporal lobe "temporal"? Cognitive neuropsychiatry, 15, 95-117.
- Dalla Barba, G., Boissé, M. F., Bartolomeo, P., & Bachoud-Lévi, A. C. (1997). Confabulation following rupture of posterior communicating artery. Cortex, 33, 563-570.
- Dalla Barba, G., Brazzarola, M., Marangoni, S., Barbera, C., & Zannoni, I. (2017). A longitudinal study of confabulation. Cortex, 87, 44-51.
- Dalla Barba, G., & Decaix, C. (2009). "Do you remember what you did on March 13, 1985?" A case study of confabulatory hypermnesia. Cortex, 45, 566-574.
- Dalla Barba, G., & La Corte, V. (2013). The hippocampus, a time machine that makes errors. Trends Cogn Sci, 17, 102-104.

- Dalla Barba, G., & La Corte, V. (2015). A neurophenomenological model for the role of the hippocampus in temporal consciousness. Evidence from confabulation. Frontiers in behavioral neuroscience, 9, 218.
- De Haan, E. H., Young, A. W., & Newcombe, F. (1991). Covert and overt recognition in prosopagnosia. Brain, 114 (Pt 6), 2575-2591.
- Dell'Acqua, F., Scifo, P., Rizzo, G., Catani, M., Simmons, A., Scotti, G., & Fazio, F. (2010). A modified damped Richardson-Lucy algorithm to reduce isotropic background effects in spherical deconvolution. Neuroimage, 49, 1446-1458.
- Dell'Acqua, F., Simmons, A., Williams, S. C., & Catani, M. (2013). Can spherical deconvolution provide more information than fiber orientations? Hindrance modulated orientational anisotropy, a true-tract specific index to characterize white matter diffusion. Hum Brain Mapp, 34, 2464-2483.
- Doricchi, F., Perani, D., Incoccia, C., Grassi, F., Cappa, S. F., Bettinardi, V., Galati, G., Pizzamiglio, L., & Fazio, F. (1997). Neural control of fast-regular saccades and antisaccades: an investigation using positron emission tomography. Exp Brain Res, 116, 50-62.
- Foulon, C., Cerliani, L., Kinkingnéhun, S., Levy, R., Rosso, C., Urbanski, M., Volle, E., & Thiebaut de Schotten, M. (2018). Advanced lesion symptom mapping analyses and implementation as BCBtoolkit. GigaScience, giy004-giy004.
- Gazzaniga, M. S. (2000). Cerebral specialization and interhemispheric communication: does the corpus callosum enable the human condition? Brain, 123 (Pt 7), 1293-1326.
- Geschwind, N. (1965). Disconnexion syndromes in animals and man Part II. Brain, 88, 585-644.
- La Corte, V., Serra, M., Attali, E., Boisse, M. F., & Dalla Barba, G. (2010). Confabulation in Alzheimer's disease and amnesia: a qualitative account and a new taxonomy. J Int Neuropsychol Soc, 16, 967-974.
- Leemans, A., & Jones, D. K. (2009). The B-matrix must be rotated when correcting for subject motion in DTI data. Magnetic Resonance in Medecine, 61, 1336-1349.
- Malhotra, P., Jager, H. R., Parton, A., Greenwood, R., Playford, E. D., Brown, M. M., Driver, J., & Husain, M. (2005). Spatial working memory capacity in unilateral neglect. Brain, 128, 424-435.
- Manning, L., & Kartsounis, L. D. (1993). Confabulations related to tacit awareness in visual neglect. Behav Neurol, 6, 211-213.
- Marshall, J. C., & Halligan, P. W. (1988). Blindsight and insight in visuo-spatial neglect. Nature, 336, 766-767.
- Papagno, C., & Baddeley, A. D. (1997). Confabulation in a dysexecutive patient: implication for models of retrieval. Cortex, 33, 743-752.
- Rees, G., Wojciulik, E., Clarke, K., Husain, M., Frith, C., & Driver, J. (2000). Unconscious activation of visual cortex in the damaged right hemisphere of a parietal patient with extinction. Brain, 123 (Pt 8), 1624-1633.
- Rojkova, K., Volle, E., Urbanski, M., Humbert, F., Dell'Acqua, F., & Thiebaut de Schotten, M. (2015). Atlasing the frontal lobe connections and their variability due to age and education: a spherical deconvolution tractography study. Brain structure & function, in press.
- Schmahmann, J. D., & Pandya, D. N. (2007). The complex history of the fronto-occipital fasciculus. Journal of the History of the Neurosciences, 16, 362-377.

- Serra, M., La Corte, V., Migliaccio, R., Brazzarola, M., Zannoni, I., Pradat-Diehl, P., & Dalla Barba, G. (2014). Confabulators mistake multiplicity for uniqueness. Cortex, 58, 239-247.
- Thiebaut de Schotten, M., Dell'Acqua, F., Forkel, S. J., Simmons, A., Vergani, F., Murphy, D. G., & Catani, M. (2011). A lateralized brain network for visuospatial attention. Nat Neurosci, 14, 1245-1246.
- Thiebaut de Schotten, M., Dell'Acqua, F., Ratiu, P., Leslie, A., Howells, H., Cabanis, E., Iba-Zizen, M. T., Plaisant, O., Simmons, A., Dronkers, N. F., Corkin, S., & Catani, M. (2015). From Phineas Gage and Monsieur Leborgne to H.M.: Revisiting Disconnection Syndromes. Cereb Cortex.
- Thiebaut de Schotten, M., Tomaiuolo, F., Aiello, M., Merola, S., Silvetti, M., Lecce, F., Bartolomeo, P., & Doricchi, F. (2014). Damage to white matter pathways in subacute and chronic spatial neglect: a group study and 2 single-case studies with complete virtual "in vivo" tractography dissection. Cereb Cortex, 24, 691-706.
- Toba, M. N., Rabuffetti, M., Duret, C., Pradat-Diehl, P., Gainotti, G., & Bartolomeo, P. (2018). Component deficits of visual neglect: "Magnetic" attraction of attention vs. impaired spatial working memory. Neuropsychologia, 109, 52-62.
- Tournier, J. D., Calamante, F., Gadian, D. G., & Connelly, A. (2004). Direct estimation of the fiber orientation density function from diffusion-weighted MRI data using spherical deconvolution. NeuroImage, 23, 1176-1185.
- Ungerleider, L. G., & Mishkin, M. (1982). Two Cortical Visual Systems. In D. J. Ingle, M. A. Goodale & R. J. W. Mansfield (Eds.), *Analysis of Visual Behavior*. Boston: MIT Press.
- Volle, E., Kinkingnehun, S., Pochon, J. B., Mondon, K., Thiebaut de Schotten, M., Seassau, M., Duffau, H., Samson, Y., Dubois, B., & Levy, R. (2008). The functional architecture of the left posterior and lateral prefrontal cortex in humans. Cereb Cortex, 18, 2460-2469.
- Vuilleumier, P., Sagiv, N., Hazeltine, E., Poldrack, R. A., Swick, D., Rafal, R. D., & Gabrieli, J. D. (2001). Neural fate of seen and unseen faces in visuospatial neglect: a combined event-related functional MRI and event-related potential study. Proc Natl Acad Sci U S A, 98, 3495-3500.
- Wansard, M., Bartolomeo, P., Bastin, C., Segovia, F., Gillet, S., Duret, C., & Meulemans, T. (2015). Support for distinct subcomponents of spatial working memory: a double dissociation between spatial-simultaneous and spatial-sequential performance in unilateral neglect. Cogn Neuropsychol, 32, 14-28.
- Wansard, M., Meulemans, T., Gillet, S., Segovia, F., Bastin, C., Toba, M. N., & Bartolomeo, P. (2014). Visual neglect: is there a relationship between impaired spatial working memory and re-cancellation? Exp Brain Res, 232, 3333-3343.
- Weiskrantz, L. (1987). Residual vision in a scotoma. A follow-up study of 'form' discrimination. Brain, 110 (Pt 1), 77-92.

FIGURE CAPTIONS

Fig. 1. Stimuli used in the experimental investigation

Fig. 2. Anatomical analysis of PC's lesion. a) Axial sections though PC's B0 diffusion image.

b) 3D reconstruction of PC's lesion in the MNI152 space. c) White matter connections

identified as damaged by the tractotron analysis. d) Brain areas identified as deafferented by

the disconnectome maps analysis. e) Tractography of the white matter connections emerging

from visual areas. f) Tractography of the perisylvian white matter connections.



















