The Lost Ability to Find the Way: Topographical Disorientation After a Left Brain Lesion

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Objective: We report the case of a patient (M.S.) who, after a left brain damage in posteromedial areas, showed a deficit in determining the direction of any destination with respect to his current position or to external frames (heading disorientation). Given that spatial cognition includes a wide range of cooperating abilities, we deemed that M.S.'s spatial disorientation could be ascribed to specific alterations within this multicomponent system where landmarks and spatial frames of reference contribute to organize information for different purposes. Method: M.S. and 12 healthy elderly people (NCs) were submitted to an extensive neuropsychological assessment and to 2 ad hoc spatial tasks: (a) Object-Location Memory Task (what, where, and their binding); and (b) spatial memory task combining categorical (nonmetric)/coordinate (metric) relations with egocentric/allocentric frames of reference (in verbal and visuomotor conditions). Results: M.S.'s performance was compared with that of NCs by means of a modified t test to small control sample size. M.S. met difficulty in positional processing and binding but not in object recognition. M.S. showed a selective deficit in the coordinate component in verbal (combined with both egocentric and allocentric frames) and visuomotor (only with the egocentric frame) spatial judgment tasks. In contrast, the categorical component looked always preserved in both frames of reference. Conclusions: The left posteromedial brain areas contribute in combining and translating metric relations according to frames of reference and in using these representations to guide actions according to an egocentric perspective.

Keywords: egocentric allocentric, categorical coordinate, topographical disorientation, object-location memory, left posteromedial brain network

Spatial disorders characterized by spatial disorientation (topographical disorientation, TD), such as getting lost or wandering, have often been described in the early stages of Alzheimer's disease (AD) or in consequence of focal brain lesions (Aguirre & D'Esposito, 1999; Burgess, Trinkler, King, Kennedy, & Cipollotti, 2006; Iachini, Iavarone, Senese, Ruotolo, & Ruggiero, 2009a; Vann, Aggleton, & Maguire, 2009). In their review, Aguirre and D'Esposito (1999) developed a taxonomy of TD by classifying these spatial disorders and related neuroanatomical lesions in four categories: (a) agnosia for landmark (inability to recognize landmarks) following damage to posterior parahippocampal-lingual region of inferior temporal cortex; (b) anterograde disorientation (inability to construct a representation of a new environment) following lesions to parahippocampal and hippocampus areas; (c) egocentric disorientation (inability to represent spatial information relative to observer's view) following bilateral or right posterior parietal impairment; (d) heading disorientation (inability to orient oneself relative to external landmarks) following impairment to retrosplenial cortex and to posterior cingulate cortex.

Although the onset of way-finding deficits can be clinically simple to identify, one problem of TD is that it does not result from a damage of a unitary cognitive function but may derive from selective deficits of one or more special functions (e.g., Burgess et al., 2006). Indeed, spatial cognition is a multicomponent system consisting of several basic abilities that must cooperate in order to subserve everyday purposes, such as finding a way in the environment and locating target positions for acting.

As widely acknowledged in the literature, our daily spatial behaviors depend on the integrity of allocentric and egocentric frames of reference (Aguirre & D'Esposito, 1999; Burgess, 2006;

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O'Keefe & Nadel, 1978; Paillard, 1991; for a review see Galati, Pelle, Berthoz, & Committeri, 2010). Egocentric frames of reference use the body or body parts (i.e., head, eyes, etc.) as anchor points to specify spatial information of the surrounding space, whereas allocentric frames of reference define the position of a target in relation to a second external element, such as an object or an environmental landmark, that acts like an anchor point (e.g., Kosslyn, 1994; McNamara, 2003; O'Keefe & Nadel, 1978; Paillard, 1991).

However, the distinction between egocentric and allocentric spatial representations is intrinsically connected to another important distinction, that is between coordinate and categorical spatial relations (Carey, Dijkerman, Murphy, Goodale, & Milner, 2006; Jager & Postma, 2003). This distinction has been first proposed by Kosslyn (1994) and refers to the level of metric precision or nonmetric invariance with which spatial relations are encoded. *Coordinate spatial relations* are based on a fine-grained metric code that allows for more precise distance discrimination between objects' positions. Instead, categorical spatial relations are based on a more abstract code that delimitates areas in the outside world in which all possible locations can be treated as more or less equivalent and provides nonmetric localizations (Carey et al., 2006; Jager & Postma, 2003; Kosslyn, 1994; Ruotolo, Iachini, Postma, & van Der Ham, 2011a; Ruotolo, van Der Ham, Iachini, & Postma, 2011b).

It has recently been demonstrated in healthy subjects that spatial frames of reference and spatial relations are different but somewhat interacting components (Ruotolo et al., 2011a; Ruotolo et al., 2011b). We cannot process metric or nonmetric spatial relations without specifying a frame of reference and, conversely, we use frames of reference always combined with spatial relations. Examples of this combination can be drawn from our daily spatial behaviors that are commonly based on spatial relations such as "the street closer to me/on my right" (egocentric) or "the building closer to the bridge/on the left of the bridge" (allocentric). Therefore, the egocentric/allocentric and the categorical/coordinate components seem likely to reflect a flexible, complex, and interactive organization that it modulated by the spatial task at hand (e.g., Kosslyn, 1994; Milner & Goodale, 2008).

Another important component of spatial cognition is *object-location memory* which is useful in maintaining a coherent and meaningful representation of the visual world and in providing a platform from which directional information can be generated (Gronau, Neta, & Bar, 2008; Postma & De Haan, 1996; Postma, Kessels, & van Asselen, 2008). Remembering the position of an object or landmark implies the capacity to process object-identity information (*what*), object-position (*where*), and the integration of both information (*what* + *where*, i.e., binding). Being able to disentangle these processes could help us to determine the efficiency of processing and combining identity and position information about landmarks around us and that represent the points of reference to trigger directional information (Moscovitch, Kapur, Kohler, & Houle, 1995).

In sum, spatial cognition includes a wide range of cooperating abilities (Iachini, Sergi, Ruggiero, & Gnisci, 2005; Postma & De Haan, 1996; Ruggiero, Sergi, & Iachini, 2008), where landmarks, spatial frames of reference, and spatial relations contribute to organize information for different perceptual and motor purposes (Coello, Bartolo, Amiri, Houdayer, & Derambure, 2008; Kosslyn, 1994; Milner & Goodale, 2008). On this basis, topographical disorientation might derive from alterations of one or more of these basic components of spatial cognition.

Here, we report data from a patient (M.S) who, as a consequence of an intracerebral hemorrhage of the left hemisphere, complained severe symptoms related to lost "sense of direction" (Aguirre & D'Esposito, 1999). More specifically, he was unable to determine the direction of unseen destinations with respect to his current position and to external landmarks that he normally recognized. As such, the symptoms he complained seemed quite consistent with the heading disorientation described by Aguirre and D'Esposito (1999; see also Ino et al., 2007; for a review, see Vann et al., 2009).

In order to verify which of the previously described components of spatial cognition was impaired, object-location memory (what, where, binding) and the combination between spatial relations (coordinate and categorical) and frames of reference (egocentric and allocentric) were investigated. There are relatively few case studies dealing with difficulty in recalling or determining directions as a consequence of left-sided posteromedial substructures lesions (e.g., involving retrosplenial and posterior cingulate cortices; for reviews, see Cauda et al., 2010; Cavanna & Trimble, 2006; Vann et al., 2009; Vogt & Laureys, 2005; Vogt, Vogt, & Laureys, 2006). In all these cases, navigational disorders were studied on the basis of map drawing of familiar places (e.g., Osawa, Maeshima, & Kunishio, 2008), mental navigation tasks (e.g., Ino et al., 2007), and clinical descriptions (e.g., Obi, Bando, Takeda, & Sakuta, 1992; see also Alsaadi, Binder, Lazar, Doorani, & Mohr, 2000; Maeshima et al., 2001; for a review, see Vann et al., 2009).

In this study, M.S. was firstly submitted to a series of classic spatial memory and environmental tasks (map drawing, pointing, route finding) to explore the nature and degree of his TD. On this basis, the patient and a matched control group were submitted to two spatial memory tasks ad hoc devised: (a) the Object-Location Memory Task investigating the role played by what, where, and what + where information in memory for object location; and (b) the Egocentric-Allocentric/Categorical-Coordinate (Ego-Allo/Cat-Coor) task investigating the combination between spatial relations (coordinate and categorical) and frames of reference (egocentric and allocentric) in order to understand which of these components was impaired and might subtend M.S.'s topographical disorders.

The Object-Location Memory Task, adapted from previous studies (Iachini et al., 2005; Laeng, 1994; Postma & De Hann, 1996; van Asselen, Kessels, Kappelle, & Postma, 2008; for a review, see Postma et al., 2008), investigates three kinds of spatial processing: (a) object-identity (*what*); (b) object-position (*where*); and (c) their binding (*what* + *where*). In the object-identity condition, participants memorized various stimuli and then, among others distracters, they had to assign the target-stimuli to their original already premarked positions. In the object-position condition, participants memorized a spatial array based on several positions occupied by the same stimuli and then they had to mark the previously studied not premarked positions. In the binding condition, participants memorized different stimuli and their related positions and then, among other distracters, they had to assign the target-stimuli to their original not premarked positions.

The Ego-Allo/Cat-Coor task is a modified version of previous behavioral paradigms (Committeri et al., 2004; Iachini & Ruggiero, 2006; Iachini, Ruggiero, Conson, & Trojano, 2009b; Ruotolo et al., 2011a; Ruotolo et al., 2011b). This task aimed at assessing the capacity to use egocentric and allocentric frames of reference in combination with categorical and coordinate spatial relations. For instance, it requires explicitly the encoding of distances (coordinate) or relations (categorical) with respect to the participant's body (egocentric) or to an external object (allocentric). This kind of experimental paradigm has already been used to assess spatial memory in healthy adults (Iachini & Ruggiero, 2006; Ruotolo et al., 2011a; Ruotolo et al., 2011b), brain damaged patients (Iachini et al., 2009b), blind people (Ruggiero, Ruotolo, & Iachini, 2009, 2012), children with cerebral palsy (Barca, Frascarelli, & Pezzulo, 2012; Barca, Pezzulo, & Castelli, 2010), in a fMRI study (Committeri et al., 2004), and has proved its efficacy in inducing a specific involvement of spatial frames of reference. In all these tasks participants kept their learning perspective during the testing phase. In classic spatial memory tasks assessing frames of reference, participants' position may remain the same during encoding and retrieval phases or may change for the testing phase (Burgess, 2006; Mou, McNamara, Valiquette, & Rump, 2004). Although spatial information is initially encoded by egocentric experiences, allocentric representations are not necessarily independent from a egocentric perspective and they can be also dependent on the individual's position, especially when it refers to relatively small environments (Grush, 2000; see also Burgess, 2006; McNamara, 2003). Overall, a facilitation of the egocentric encoding over the allocentric one has been reported: Allocentric accuracy ranges from 37% to 60% and egocentric accuracy from 70% and over (Pouliot & Gagnon, 2005).

Participants memorized triads of three-dimensional (3D) geometrical objects and, after a delay, they provided the combined egocentric-allocentric and coordinate-categorical spatial judgments by means of verbal and visuomotor response modalities. The choice to adopt different response modalities is inspired by evidence showing that frames of reference may be differently affected by a response requiring visual control of action and a response only requiring verbal judgments (Carey et al., 2006; Frassinetti, Bonifazi, & Làdavas, 2007; Heath, Rival, Neely, & Krigolson, 2006).

Finally, according to the classical neuropsychological approach, the correlation between M.S.'s lesion and his deficits at behavioral level was investigated to achieve some information about the neural structures involved in processing basic spatial components and, consequently, in spatial orientation.

Method

Case Study

The patient (M.S.) was a 69-year-old right-handed man. Education and handedness (Oldfield, 1971) are reported in Table 1. He was a retired air traffic controller officer in the Italian Air Force who was reported (by his daughters) as having excellent memory and capacity to solve logic, puzzle, and math games. Family history was negative for cognitive and behavioral disorders, nor any kind of cognitive or affective complaints were reported by the patient. M.S. showed an intracerebral hemorrhagic episode characterized by headache, transitory right visual field deficit, and pronounced disorders of spatial orientation. After the stroke episode, he was led to Neurological and Stroke Unit, CTO Hospital (Naples). Once there, he was submitted to a brain CT scan showing a hyperdense lesion involving left postero-medial areas. The lesion was surrounded by edema but without signs indicating a subarachnoid component of the hemorrhage. The patient underwent medical therapy aimed at reducing blood pressure and edema. A few days after, a new brain CT scan confirmed the hemorrhage, the absence of blood in the subarachnoid space, and incoming reduction of the edema. About 6 months after the onset of the stroke, M.S. was submitted to a brain MRI because of his persistent and stable spatial orientation disorders. The brain MRI showed a unilateral and focal lesion involving the parahippocampal gyrus, the posterior cingulate gyrus, and the precuneus in the left hemisphere (see Figure 1) without neuroimaging signs of overt vasculopathy.

Within the next 6 weeks, M.S.'s general cognitive functioning and spatial memory disorders were assessed. During the neurological and neuropsychological assessment the patient appeared fully oriented in time and space and was very cooperative throughout the testing period. Neurological examination did not show hemiparesis, somatosensory deficits, or clinical signs of contralesional extinction on visual and tactile bilateral stimulation. Visual field deficits due to optic nerve or neurological lesions were excluded by means of a computerized perimetry. Ophthalmological assessment also indicated an intact stereoscopic depth perception. There was no sign of intention tremor and hypermetric errors in the classical clinical testing of finger–nose pointing. He exhibited no difficulty in reaching for objects or in manipulating them and he did not show confusion between his own limbs or between those of the examiner's.

M.S. was submitted to an extensive neuropsychological assessment. On the whole, the assessment did not disclose impairments in intellectual, language, visuoperceptual and visuospatial skills (see Table 1). He showed normal ability to imitate with the right hand different gestures performed by the experimenter. He could recognize everyday newspapers, familiar faces (5/5), famous buildings (5/5), and landscapes (5/5) of his city (Naples). His spontaneous speech was fluent, and his language comprehension was good as well as his reading and writing. He could accurately perform line bisection and copy model drawings. He only reported long-term verbal memory difficulty (i.e., story retell and delayed Rey's list). Moreover, he achieved a normal score on the Three-Objects-Three-Places test, a test evaluating long-term visuospatial memory for the screening of AD (Prestia et al., 2006).

Critically, M.S. referred that while walking alone around his quarter, he realized to be unable to return to his house and wandered around for a while. Although he recognized some points of reference, these landmarks did not trigger directional information about other places, regardless of the level of familiarity with the environment (e.g., Iachini, Ruotolo, & Ruggiero, 2009c). Indeed, the patient could not even determine the route between highly-familiar positions (e.g., from his daughters' houses to his own house). As a consequence of this spatial disorder, M.S. stopped to drive and was able to walk alone only in a small set of very well-known surroundings. The referred symptoms suggest a topographical disorientation with a severe and negative impact on patient's daily life so to heavily limit his autonomy.

In order to understand the characteristics of his spatial disorientation, M.S. was asked to perform environmental spatial

Table	1	
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Demographic Data, Scores and Cut-Off Levels on the Neuropsychological Tests for M.S. and Normal Controls (NCs)

		NC	
	M.S.	Mean	SD
Age (years)	69	69.1	1.9
Education (years of schooling)	17	17.25	0.62
Edinburgh Handedness Inventory (-100/+100)	+ 90	+ 8	8
Neuropsychological tests	M.S.'s score	Cut-off levels	
MMSE	27.30	24	
MDB			
Immediate Visual Memory test	14.20	13.85	
Phonological verbal fluency	36.50	17.35	
Sentence Construction test	23.70	8.72	
Rey Auditory Verbal test: immediate recall	30.30	28.85	
Rey Auditory Verbal test: delayed recall	3.80^	4.69	
Raven's colored progressive matrices	21.40	18.96	
Copy of Drawings test	8.40	7.18	
Copy of Drawings with landmarks	68.30	61.85*	
ENPA	(7 subsets)		
Additional neuropsychological tests			
Verbal span	6	3.75	
Story retell	6^	7.5	
Token test	34	26.5	
Visual discrimination task	32	21	
Attentional matrices	42.3	31	
FAB	16.58	12.03	
Corsi Block tapping test	4.4	3.50	
Stroop test (RTsec/Accuracy)	31/3.6	36.9/4.23	
>Three-Objects-Three-Places test	8	6–7	
BVA			
Line length discrimination test		$t = -2.193, p = .22^{**}$	
Angle size test		$t = -0.696, p = .50^{**}$	

Note. MDB = Mental Deterioration Battery (Carlesimo, Caltagirone, & Gainotti, 1996); ENPA = Neuropsychological Examination for Aphasia (Capasso & Miceli, 2001); FAB = Frontal Assessment Battery (Dubois, Slachevsky, Litvan, & Pillon, 2000; Iavarone et al., 2004); BVA = Battery for Visuospatial Abilities and Additional neuropsychological tests (Barletta-Rodolfi, Ghidoni, & Gasparini, 2011).

^ The performance is under the cut-off level. * M.S.'s performance was above the cut-off levels for all assessed subsets. ** The difference is not statistically significant according to Crawford and Garthwaite's (2002) test.

tasks that are usually used in the literature to assess TD, such as map-drawings, route finding, and spatial pointing tasks (e.g., Ciaramelli, Rosenbaum, Solcz, Levine, & Moscovitch, 2010; Hashimoto, Tanaka, & Nakano, 2010; Ino et al., 2007). Overall, he showed several difficulties in these tasks.

Patient's Lesion Description

A brain MRI with angio-MRI was performed to better define the characteristics of the hemorrhage and to clarify the possible mechanisms underlying the stroke. The imaging excluded that hemorrhage could be due to a brain tumor, aneurism, or artero-venous angioma.

MRI digitalized image of patient M.S. was mapped using MRIcro software (Rorden, 2011). Patient's focal lesion visible on MRI scan was manually traced onto corresponding regions of a normal reference brain (template). Figure 1 represents template slices corresponding to MRI scan slices in which lesion was visible. For each template slice, the absolute center of the mapped lesion in Talairach and Tournoux (1988) coordinates was identified. By means of Talairach's coordinates the area involved by the lesion for each slice was identified. As described in detail in Figure 1, the regions maximally involved by the patient's lesion were the parahippocampal gyrus (Brodmann area, BA 30; Brodmann, 1909), the posterior cingulate gyrus (BA 30), and the precuneus (BA 31) in the left hemisphere. MRI scan did not show neuroimaging signs of overt vasculopathy (Fazekas score < 2).

Healthy Participants

The performance of M.S. was compared with that of 12 righthanded male participants, matched in terms of age, education, and handedness (Oldfield, 1971), as reported in Table 1, without history of neurological or psychiatric disease. The criteria for exclusion from the study were the presence of cognitive impairments (score lower than 24 at the Mini-Mental State Examination [MMSE]; Folstein, Folstein, & McHugh, 1975; Iavarone et al., 2007). All participants, including M.S., gave their informed consent to participate in the study, which was approved by the local ethics committee. All procedures were in agreement with the 1975 Helsinki Declaration.



Figure 1. Patient's lesion map reconstructed by using MRIcro software on a template brain, in axial and sagittal view. Areas marked with gray represent those involved by the lesion. For each axial slice the absolute centre of the lesion by Talairach's coordinates and areas involved by the lesion for each slice were identified. Talairach's coordinates and BA areas: Left Limbic lobe (BA30), Parahippocampal Gyrus (x = -18, y = -51, z = 2), Posterior Cingulate Gyrus (x = -13, y = -51, z = 10; x = -12, y = -55, z = 14); Left Parietal Lobe (BA31), Precuneus (x = -11, y = -57, z = 18; x = -11, y = -67, z = 22).

Assessment of M.S.'s Topographical Disorientation

Patient's TD was assessed by means of spatial tasks that required spatial memory for indoor/outdoor familiar/unfamiliar environments: (a) map-drawings, (b) pointing tasks, and (d) route finding tasks (see Ciaramelli et al., 2010; Hashimoto et al., 2010; Ino et al., 2007; Vann et al., 2009).

Map drawing of indoor environments. M.S. was asked to draw a sketch-map of his large apartment. The accuracy, that is, the correct rooms (seven in number) and their related positions, was measured (correct = 1, incorrect = 0; range = 0-7). M.S. reproduced his apartment with good approximation, but reversed the position of two rooms (5/7). M.S. had also to draw a sketch-map of a floor of the hospital (range = 0-10); in this case he was severely impaired (1/10).

Map-drawing of outdoor environments. M.S. was invited to draw the configuration of the main surrounding streets of his quarter and hospital area. The accuracy (i.e., 1 assigned to each part of the map correctly reproduced) was scored by means of a city map of Naples. His quarter was poorly sketched with only two lines connecting his daughters' houses and the neighboring square (2/8). Instead, he was unable to perform the map drawing of the unfamiliar hospital area.

Pointing tasks. M.S. was asked to perform pointing tasks either in familiar (his apartment) or unfamiliar (hospital) places. In both cases, he was required to memorize eight landmarks placed at different angular degrees from 0° (his facing position) to 360° (e.g., 0°, 45°, 90°, and so forth; with a step of 45°). After memorizing, he had to point to unseen positions according to the classic pointing task procedure, that is, "You are here, facing Y, point to Z" (see McNamara, 2003). For each pointed position, accuracy was assigned (1 = correct, 0 = incorrect; range = 0–8). A pointed position was considered correct if it fell within the same quadrant of the exact position. M.S. pointed roughly to the correct positions at home (8/8) but not in the hospital (3/8) places.

Indoor route finding tasks. M.S. was invited to recall route information from his current position toward three different target positions in the hospital floor and in the building where he lived. For example, he was asked to describe "How do you go from your current position to the infirmary as if you were walking through?" He was unable to recall the route between these positions involving two left turns and three right turns or vice versa, even after several days of hospitalization. For each correct position, the accuracy was assigned (correct = 1, incorrect = 0; range 0-5 for route). M.S.'s performance appeared drastically impaired in both environments (familiar routes = 4/15; unfamiliar routes = 0/15).

Outdoor route finding tasks. M.S. was led to familiar (little square close to his home) and unfamiliar (parking of hospital area) places. He had to describe as accurately as possible how to get from his current position toward unseen surroundings places as if he was walking through. The questions regarded three neighboring routes (average length of each one about 600 m/700 m). The accuracy was checked by means of a city map of Naples (correct = 1, incorrect = 0; range 0-5 for route). Patient performed negatively in both tasks (familiar routes = 3/15; unfamiliar routes = 2/15).

Ad Hoc Spatial Memory Tasks

Patient and NCs were tested on two ad hoc devised spatial memory tasks: (a) the Object-Location Memory Task and (b) the Ego-Allo/Cat-Coor task.

Object-Location Memory Task

This task was devised on the basis of the studies carried out by Postma and De Hann (1996; Iachini et al., 2005; Laeng, 1994; van Asselen et al., 2008; for a review see Postma et al., 2008). The task consisted of three subsets: an identity task (*What*), a position task (*Where*), and an object-to-position task (*What* + *Where*: binding information).

Black and white stimuli were selected on the basis of the following criteria: (a) target stimuli and distracters belonged to the same categories (animals and objects); (b) absence of phonemic overlapping; and (c) all stimuli were comparable on the basis of the number of syllables and frequency of occurrence (Bortolini, Tagliavini, & Zampolli, 1971).

Participants were asked to study (20 sec) a number of stimuli (from two to seven) depicting highly familiar animals and objects (e.g., chair, bird, etc.). The stimuli were reported in a squared frame (15×15 cm) on a sheet. Then, the sheet was removed and after 5 sec the testing phase took place.

Identity task (What). Participants had to memorize different types of stimuli and then, once removed the sheet, they were

shown with a squared frame with highlighted gray squares (premarked positions) indicating the positions previously occupied by the stimuli. Below it, target- and distracter-stimuli (paired in kind of category), with a number at their top, were randomly distributed in two rows. Participants had to recognize the targetstimuli and assign their corresponding number to their original premarked positions.

Position task (Where). A squared frame showing one kind of stimulus per trial (e.g., ball), occupying several positions, was presented. After memorizing the spatial array, participants were presented with a sheet with an empty squared frame and below it the only stimulus previously presented. Participants had to mark (with a "X") the positions previously occupied by the stimulus.

Object to position task (What + Where). Participants had to memorize different stimuli occupying different positions. Afterward, participants were presented with a sheet comprising an empty squared frame and below it target- and distracter-stimuli (paired in kind of category) that were randomly distributed in two rows. Each stimulus was matched with a number at their top. Participants had to recognize the previously studied target-stimuli among distracters and assign their corresponding number to their original not premarked positions.

The task lasted about 25 minutes. For each subtask, accuracy was scored. In the position and in the object to position conditions a see-through sheet made by a 5×5 matrix was overlapped to the frame with participants' answers. If the answer was outside the correct box, it was scored 0, if it was inside the correct box it was scored 1. For each subtask, we had a total of 27 possible correct responses (score range = 0–27). The order of presentation of the three subtasks was balanced among participants. Within each subtask, the order of presentation of trials was randomized.

Ego-Allo/Cat-Coor Task

This task explicitly manipulates the spatial combinations by requiring the encoding of metric distances (coordinate) or relational (categorical) with respect to the participant's body (egocentric) or to an external object (allocentric). After having memorized a triad of objects placed at different positions from each other and from the participant's body, participants were asked to provide four kinds of spatial judgments representing each combination.

The experiment took place in a sound-proofed comfortable room. Participants sat in front of a small desk where the stimuli were presented on plasterboard panels. The stimuli were the same used by Iachini and colleagues (Iachini & Ruggiero, 2006; Iachini et al., 2009b; Ruggiero et al., 2012). They comprised six easily nameable actual geometrical objects (pyramid, parallelepiped, cone, cube, sphere, and cylinder). They varied in color (dark/ medium/light gray) and size: big objects (8 cm \times 8 cm; except parallelepiped and cylinder: 8 cm \times 11 cm) and small objects (6 $cm \times 6$ cm; except parallelepiped and cylinder: 6 cm \times 9 cm). By combining these features, 24 triads were obtained. To ensure that all triads were presented in the same way, 24 plasterboard panels (each one measuring 50 cm \times 30 cm, 2 cm of thick) of the same size of the desk were used. On each panel, the shape forming the base of each object was engraved and the corresponding object was placed there. Each triad was arranged on the corresponding panel according to the following criteria: (a) interobject metric distances had to be easily distinguishable and (b) the metric distances were established in such a way that the amount of metric difficulty was the same for egocentric and allocentric judgments.

Participants were first given written instructions describing the experimental procedure, then there was a training session by using three common objects (e.g., a glass, a cup, and a small box). Afterward, all experimental stimuli were presented and participants had to name them. In this way, difficulties due to naming problems could be excluded. Finally, the experiment started.

Learning phase. Participants had to memorize (6 sec) the three objects and their positions presented on the panel. Afterward, they had to close their eyes while the experimenter removed the triad (5 sec). Then, the testing phase began (see Figure 2).



Figure 2. Example of setting and materials of the Ego-Allo/Cat-Coor task. On the *left*, a triad used for the learning phase is shown. The black dashed lines indicate the plasterboard panel placed on the desk. On the *right*, the visuomotor response modality is illustrated. The black dashed lines indicate the blank paper covering the desk.

Testing phase (Verbal response modality). After learning each triad, participants were asked to verbally provide one of four types of spatial judgments (24 judgments for 24 triads) in response to four kinds of questions: (a) egocentric-coordinate (Ego-Coor), "Which object was closest/farthest to you?"; (b) egocentriccategorical (Ego-Cat), "Which object was on your left\right?"; (c) allocentric-coordinate (Allo-Coor), "Which object was closest/ farthest to a target object (e.g., cilinder)?"; and (d) allocentriccategorical (Allo-Cat), "Which object was on the left\right of the target object (e.g., cilinder)?". For each judgment accuracy (1 = correct; 0 = incorrect; score range = 0–6 for each spatial combination) was recorded. The mean accuracy per subject was computed.

Testing phase (Visuomotor response modality). After memorizing each triad, participants had to provide visuomotor judgments in response to four kinds of questions: (a) egocentriccoordinate (Ego-Coor), "Where was the object closest to you?"; (b) egocentric-categorical (Ego-Cat), "Where was the cube with respect to you?"; (c) allocentric-coordinate (Allo-Coor), "Where was the object closest to the target (e.g., cilinder)?"; and (d) allocentric-categorical (Allo-Cat), "Where was the cilinder with respect to the target (e.g., pyramid)?". During the 5 sec delay between learning and testing, the panel was removed and a blank paper was placed on the desk. By using the index finger of their dominant arm, participants had to point and touch on the blank paper the position previously occupied by the center of the target object. Each blank paper was exactly of the same size as the desk. Once participants touched the required position, the experimenter marked immediately the pointed position on the paper (see Figure 2).

Two measures were scored: absolute metric error (cm) and accuracy (0/1, score range = 0-6 for each spatial combination). The mean accuracy per subject was calculated. The metric error corresponded to the distance in cm between original and estimated positions of each target. The absolute value was considered. Moreover, in order to compare this metric measure with the percentage of accuracy used in the verbal condition, we worked out a similar measure by following this criterion: estimated positions distant more than 8 cm from the center of the target object were scored 0, those distant less than 8 cm were scored 1. For each response modality, the order of presentation of the questions was first randomized and then balanced across subjects.

Results

M.S.'s performances on Object-Location Memory Task (mean accuracy) and on Ego-Allo/Cat-Coor tasks for both verbal (mean accuracy) and visuomotor (mean accuracy and absolute metric error) response modalities were measured. Then, for each condition, patients' performance was compared with NCs' performance by means of a modified *t* test to small control sample size (Crawford & Howell, 1998; Crawford & Garthwaite, 2002).¹ We used one-tailed tests because the null hypothesis was that M.S. would have performed better than the control group in both accuracy and metric error (e.g., Carey et al., 2006).

Object-Location Memory Task

Patient's and controls' accuracy in the three subtasks is illustrated in Figure 3. **Identity task.** M.S. showed a similar accuracy as compared with NCs in recognizing the correct stimuli (respectively 88.9% vs. 79.6%; t = 0.602, p = .28).

Position task. In contrast, M.S. was less accurate than NC in localizing the position of stimuli (48.1% vs. 73.4; t = -3.095, p < .009).

Identity to position task. Again, when the identity of an object had to be associated with its position, M.S. revealed difficulties with respect to NCs (37% vs. 62.7%; t = -2.261, p < .033).

Ego-Allo/Cat-Coor Task

Verbal response modality (Accuracy). M.S. was less accurate than NC in egocentric-coordinate (17% vs. 83%; t = -2.882, p < .007) and allocentric-coordinate (17% vs. 78%; t = -2.254, p < .023) spatial judgments (see Figure 4). In categorical spatial judgments, patient's and NCs' performances were not significantly different in egocentric (83% vs. 86%; t = -0.170, p = .43) as well as allocentric (100% vs. 75%; t = 0.961, p = .18) frames. These data suggest that M.S. was impaired in providing spatial judgments when coordinate relations, and not categorical relations, were combined with egocentric and allocentric frames of reference.

Visuomotor response modality (Accuracy). In egocentriccoordinate spatial judgments, patient's performance was impaired as compared with the corresponding condition in NCs (17% vs. 75%; t = -1.922, p < .04), as shown in Figure 5. In allocentriccoordinate spatial judgments, although the patient performed worse than NCs', this difference was not significant (34% vs. 56%; t = -0.641, p = .27). In categorical spatial judgments, M.S. and NCs were not significantly different in egocentric (67% vs. 75%; t = -0.265, p = .40) as well as allocentric (50% vs. 67%; t = -0.510, p = .31) frames.

Visuomotor response modality (Absolute metric error). As illustrated in Figure 6, the pattern of data based on absolute metric distance confirmed what previously observed. In egocentric-coordinate spatial judgments, M.S. made higher metric errors than NCs (13.5 cm vs. 6 cm; t = 2.446, p < .03). In allocentric-coordinate spatial judgments, M.S.'s and NCs' performances were not significantly different (12.74 cm vs. 9.5 cm; t = 0.560, p = .29). In categorical spatial judgments, patient's and NCs' metric errors were not significantly different in egocentric (7.34 cm vs. 8.02 cm; t = -0.135, p = .45) as well as allocentric (9.6 cm vs. 6.98 cm; t = 0.902, p = .19) frames.

¹ As regards approaches used in single-case studies, a common method is to convert the patient's score to a z-score based on the mean and SD of the NCs (Crawford & Garthwaite, 2005). However, as highlighted by Crawford and colleagues (Crawford & Garthwaite, 2002; Crawford & Howell, 1998; Crawford & Garthwaite, 2005), this approach treats the normal sample as if it was a population and, therefore, the related mean and SD are used as parameters rather than sample statistics; furthermore, the small size of NC samples (ranging from 2 to 20) makes this method of data analysis not suitable (Crawford & Garthwaite, 2002; Crawford & Howell, 1998). Instead, Crawford's procedures use the t-distribution (with n-1 degrees of freedom) rather than the standard normal distribution to estimate the abnormality of the patient's score and to test whether it is significantly lower than NCs' score. According to these authors, this modified t-test provides a more appropriate statistical analysis for single-case studies and is more robust to violations of normality (Crawford, Garthwaite, Azzalini, Howell, & Laws, 2006).



Figure 3. Accuracy of the Object-Location Memory task for Identity (*what*), position (*where*) and identity + position (*what* + *where*, i.e. binding) information, in patient (M.S.) and normal controls (NCs).

Discussion

In the present study distinct spatial components, that is, what, where, and what + where of object-location memory, and spatial relations (categorical/coordinate) combined with frames of reference (egocentric/allocentric) of memory-based spatial judgments, were investigated in a brain damaged patient (M.S.). He showed a normal performance on all of the neuropsychological assessment measures, with the exception of a modest performance on the delayed verbal recall tasks. This behavior leads us to hypothesize a retrieval difficulty more than a storage disorder when delay takes at least 10 min. Indeed, M.S. was able to identify the correct items among distractors (i.e., 13/15 words belonging to the Rey's word list) with no evidence of false alarms. From the other hand, an encoding disorder could be likely excluded because he normally performed the verbal span test. Furthermore, the absence of confabulation allows us to rule out, along with normal performances at tests for frontal lobes, an additional executive impairment.

Despite his good performance on neuropsychological tests, however, the most clinically relevant symptom was his inability to produce directional information with respect to his current position



Figure 4. Accuracy in the verbal response task in Egocentric (Ego)/Allocentric (Allo) and Categorical (Cat)/Coordinate (Coor) spatial judgments, in patient (M.S.) and normal controls (NCs).



Figure 5. Accuracy in the visuo-motor response task in Egocentric (Ego)/Allocentric (Allo) and Categorical (Cat)/Coordinate (Coor) spatial judgments, in patient (M.S.) and normal controls (NCs).

and to external landmarks (Aguirre & D'Esposito, 1999; Hashimoto et al., 2010; Ino et al., 2007; Vann et al., 2009). Performance on the spatial tasks about familiar/unfamiliar and indoor/outdoor environments clearly showed that M.S. had difficulty in pointing tasks (in unfamiliar places) that required the ability to connect external positions to his current position, in route finding tasks that required the ability to retrieve spatial relationships between external routes starting from his egocentric position, and finally in map drawing that implied the capacity of building up a configurational representation of space. However, in all these

tasks the egocentric and allocentric components can be used in cooperation: For example, one can imagine a first-person route as aid to draw a map or can try to retrieve the position of a target in relation to a second external target to support a pointing judgment (see Neggers, van der Lubbe, Ramsey, & Postma, 2006). Moreover, environmental knowledge always implies landmarks. The results obtained from the ad hoc spatial tasks contributed to clarify the "nature" of patient's deficit.

Results from the Object-Location Memory Task showed that the patient had no problem in recognizing object identities (landmarks)



Figure 6. Absolute metric error in the visuomotor response task in Egocentric (Ego)/Allocentric (Allo) and Categorical (Cat)/Coordinate (Coor) spatial judgments, in patient (M.S.) and normal controls (NCs).

but he had difficulty in retrieving their positions and in binding identities and positions (Postma et al., 2008). Therefore, the patient revealed an impairment with the spatial-positional component of the task that could also explain his difficulty in the binding process. The literature about object-location memory has shown a decline on the binding component as compared to object recognition and position processing with ageing (see Kessels, Boekhorst, & Postma, 2005; Kessels, Hobbel, & Postma, 2007; Schiavetto, Köhler, Grady, Winocur, & Moscovitch, 2002). The same trend seems to characterize our control group (see Figure 3). Instead, M.S. performed even slightly better than normal controls in recognizing object identities, whereas his performance worsened in positional memory. This would suggest that the lesioned areas play an important role in processing the where and, as a consequence, this impairment may negatively influence the *what* + *where* processing of object-location memory. As regards the hemispheric specialization of coordinate versus categorical processing, few studies have shown a deficit in object-coordinate position binding in left brain damaged patients (Kessels, de Haan, Kappelle, & Postma, 2002a; Kessels, Kappelle, de Haan, & Postma, 2002b; Kessels, Hendriks, Schouten, Van Asselen, & Postma, 2004). In the ongoing debate about the neural bases of object-location memory (e.g., Abrahams, Pickering, Polkey, & Morris, 1997; van Asselen et al., 2008; for a review, see Postma et al., 2008) our findings support the hypothesis of a crucial role of the left hemisphere in the where and what + where components (see Postma et al., 2008).

Therefore, the first task confirms a deficit in the spatial processing of object-location memory and excludes an impairment in the capacity to recognize landmarks. However, which spatial subcomponents are responsible for patient's impairment?

Spatial location memory may reflect the aggregated influences of both coordinate and categorical codes (e.g., Huttenlocher, Hedges, Corrigan, & Crawford, 2004) and egocentric and allocentric frames (Bachtold, Brugger, & Regard, 2000; Postma et al., 2008). Therefore, a task that required the combination of coordinate-categorical relations with egocentric-allocentric frames was necessary to determine which underlying component(s) could be disrupted. The results showed a selective deficit in the coordinate component in verbal (combined with both egocentric and allocentric frames) and visuomotor (only with the egocentric frame) spatial judgment tasks. In contrast, the categorical component looked always preserved in both frames of reference. How can we explain this pattern of data? One possibility is that the absence of severe verbal problems could have contributed to preserve categorical processing (Postma et al., 2008). Previous literature suggests a similarity between categorical processing and object identity processing (Jager & Postma, 2003; Kosslyn, 1994). Experimental evidence has shown that verbalization processes are involved in encoding categorical spatial information and object identity (Dent & Smyth, 2005; Postma & De Hann, 1996; Postma et al., 2008). M.S. performed efficiently in both categorical processing and object recognition: This may imply that more abstract and invariant spatial processes are preserved.²

For example, in their neurofunctional study of mental navigation, Ino et al. (2007) reported the case of a patient who was unable to determine any direction according to frames of reference as a consequence of a lesion of the left postero-cingulate/retrosplenial region. Their patient was asked to mentally move from a first to a second position in familiar and unfamiliar environments and he could not perform the task. The authors concluded that these posteromedial areas play a key role in producing directional representations according to both egocentric and allocentric systems (Aguirre & D'Esposito, 1999; Burgess, 2008; see also Byrne, Becker, & Burgess, 2007; Vann et al., 2009). More closely related to our task, Iachini, Ruggiero, Conson, and Trojano (2009b) found that left brain damaged patients were impaired in both egocentric and allocentric verbal judgments of coordinate distance, whereas right brain damaged patients showed a dramatic deficit only in the egocentric encoding. Although the categorical component was not investigated in the mentioned study, the results suggested that the left hemisphere contributes to the processing of coordinate spatial information according to frames of reference.

Instead, in the visuomotor condition, M.S. showed a significant impairment only in the egocentric-coordinate spatial encoding (coherently in both measures: metric errors and accuracy), yet the difficulty was mitigated in the allocentriccoordinate encoding. Clearly, this condition emphasizes the importance of the egocentric component because visuomotor control is needed to guide the hand toward the target location (e.g., Bruno & Franz, 2009; Milner & Goodale, 2008). Speculatively, if we put verbal and visuomotor response modalities along a continuum from a no-action-oriented task (i.e., verbal condition) to an action-oriented task (i.e., visuomotor condition), we can hypothesize that the verbal condition would mainly require to retrieve spatial information from memory and to compare metric distances by resorting to visuospatial imagery processes. Instead, it is necessary to translate memorized information into egocentric effector-based coordinates in order to give a visuomotor response. Therefore, this specific impairment is consistent with evidence attributing a crucial role to posteromedial brain areas in translational processes between spatial frames (Burgess, 2008; Byrne et al., 2007). These processes should involve a structure that is able to direct attention in space, to inspect internal spatial representations and to compare them in order to construct ongoing effector-based coordinates (Cabeza, Ciaramelli, Olson, & Moscovitch, 2008; Ciaramelli et al., 2010; Fletcher et al., 1995). As suggested in the literature, a candidate structure within posteromedial areas

The coordinate difficulty in combination with the frames of reference was affected by the response modality. In the *verbal condition*, M.S.'s spatial deficit penalizes severely the metric component associated with both frames of reference. This pattern of data is in line with few case-studies reporting topographical disorders in presence of left-sided lesions (Alsaadi et al., 2000; Ciaramelli et al., 2010; Ino et al., 2007; Maeshima et al., 2001; Obi et al., 1992; Osawa et al., 2008; Valenstein et al., 1987).

² However, one may argue that the distance judgment is not a truly coordinate task and that, simply, a different categorical level is assessed. The distinction between the two classes of spatial relations is not dichotomous but, along a continuum, is defined by the level of precision required by the spatial task: from exact metric position to closer/farther judgment to a "larger than a given magnitude" judgment to left/right judgment (for reviews, see Jager & Postma, 2003; Pouliot & Gagnon, 2005). The coordinate judgment used in this study (which can also be called proximity judgment, e.g., Ciaramelli et al., 2010) requires a discrimination between different distances. The categorical judgment, in contrast, only requires to assign a position to a class of equivalence such as left/right irrespectively of distances. In other words, it focuses on relational and invariant spatial information (Jager & Postma, 2003; Kosslyn, 1994; Ruotolo et al., 2011a).

could be the left precuneus, a dorsal structure implied in several highly integrated tasks (i.e., attention, working memory, spatially guided behaviors, visuospatial imagery processes) and thought to decide whether a response can utilize contextual spatial information in cooperation with self-referential and memory-related imagery functions (Cauda et al., 2010; Cavanna & Trimble, 2006; Dörfel, Werner, Schaefer, von Kummer, & Karl, 2009).

Therefore, the visuomotor condition might have stressed M.S.'s impairment related to his difficulty to trigger egocentrically based actions. To reach an object or a position, it is important to compute their location relative to our arm and hand (arm- and hand-centered coordinates). These egocentric frames should be particularly important in planning and performing reaching movements (Caminiti, Johnson, Galli, Ferraina, & Burnod, 1991; Kalaska & Crammond, 1992; Tipper, Lortie, & Baylis, 1992). For this reason, the visuomotor condition underlines the patient's deficit according to egocentric rather than allocentric frames. However, the overall data suggest that the frames of reference may be selectively affected by the lesioned site depending on their combination with categorical and coordinate spatial codes and on the required response modality.

In short, three considerations can be drawn from the pattern of results. First, as regards object-location memory, M.S. showed a difficulty in positional processing and object to position binding but not object identity recognition. Second, the failures in spatial performances can be ascribed by a large amount to a deficit in processing coordinate information according to both frames of reference. Third, a specific difficulty is observed when a visually guided hand action toward a target position on the basis of egocentric and coordinate information is required.

These considerations bear on the nature of M.S.'s spatial disorders. They can be attributed to a difficulty in translating memorized spatial information into egocentric body-based frames to visually guide action in space. The latter is in line with the so-called *translational function*, that is, transferring memorized spatial information according to navigational purposes, attributed to posteromedial substructures and in particular to the retrosplenial cortex (Burgess, 2008; Byrne et al., 2007; Vann et al., 2009; Vogt et al., 2006). Moreover, neurofunctional evidence has shown that a similar network (precuneus/posterior cingulate/retrosplenial network), mainly localized in the left hemisphere, is involved in retrieving contextual visuospatial information (Dörfel et al., 2009; Ghaem et al., 1998; Wang et al., 2010), in processing visually guided behaviors (Wenderoth, Debaere, Sunaert, & Swinnen, 2005) and hand-object interactions (Vingerhoets, 2008).

Therefore, it is likely that M.S.'s left lesion involving the parahippocampal gyrus, the posterior cingulate gyrus (including the retrosplenial cortex) and the precuneus would determine a difficulty in combining coordinate spatial relations with frames of references and in translating allocentric into egocentric frames and vice versa depending on the spatial purpose. When required to use this information for acting, the patient should meet severe difficulties in working out egocentric coordinates to guide action. The behavioral consequence of this alteration should be a difficulty in finding the way toward both familiar and unfamiliar places.

As regards to M.S.'s TD, his neuropsychological characteristics look compatible with heading disorientation (Aguirre & D'Esposito, 1999; Vann et al., 2009). However, heading disorientation can be attributed to alterations of both spatial frames of reference, as also suggested by Aguirre and D'Esposito (1999; Hashimoto et al., 2010; Ino et al., 2007). The present results suggest that the core of M.S.'s TD may consist in a difficulty in combining and translating egocentric/allocentric coordinate frames of reference, and in using these representations to guide actions according to an egocentric perspective.

Finally, for clinical purposes, the tests proposed here may be useful to detect which specific spatial subcomponents are impaired in patients with spatial disorientation disorders and to set up ad hoc rehabilitative treatments.

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