



## Long-lasting topographical disorientation in new environments

Maria Luisa Rusconi <sup>a,\*</sup>, Francesca Morganti <sup>a,b</sup>, Anna Paladino <sup>a,c</sup>

<sup>a</sup> Department of Human Sciences, University of Bergamo, Italy

<sup>b</sup> Applied Technology for Neuro-Psychology Lab, Istituto Auxologico Italiano, Milano, Italy

<sup>c</sup> Department of Neurological Sciences, University of Milan, Fondazione Ospedale Maggiore Policlinico, Italy

### ARTICLE INFO

#### Article history:

Received 19 December 2007

Received in revised form 11 June 2008

Accepted 13 June 2008

Available online 24 July 2008

#### Keywords:

Topographical disorientation

Anterograde topographical amnesia

Spatial cognition

Spatial learning

Hippocampus

### ABSTRACT

We describe the case of a young woman with long-lasting topographical disorientation following a haemorrhagic lesion of the right temporo-occipital region involving the hippocampus. She was unable to orient herself in novel environments and to perform learning spatial tasks both in real-world settings and laboratory conditions. Her ability to recall and navigate through known routes as well as to recognize familiar landmarks was preserved. Neuropsychological evaluation revealed a mild long-term memory deficit. A similar neuropsychological and experimental pattern was observed 8 years later (at the time of follow-up) when she showed a persistent topographical disorientation and a slight worsening of verbal and visuo-spatial long-term memory disorders. Her topographical disorientation was characterized by an impairment confined to the anterograde memory domain, a not frequent pattern reported in literature, in the absence of remote topographical memory disorders. The presence of a lesion localized in the right occipito-temporal region and hippocampus combined with the results observed in some experimental tasks could also contribute to the debate of the role of neural correlates involved in topographical spatial knowledge.

© 2008 Elsevier B.V. All rights reserved.

### 1. Introduction

Topographical disorientation (TD) is characterized by the inability to navigate through familiar or unfamiliar environments. Patients affected by this type of spatial disorder may not be able to recall familiar routes or to learn novel routes. In literature, different types of TD have been described and classified under two major categories [1–5]: topographical agnosia and topographical amnesia, a dichotomy that remains somewhat unclear.

Topographical agnosia (see for example, [6]) has been typically described as a perceptual difficulty to identify and recognize landmarks (places, buildings, landscapes, streets etc.).

Topographical amnesia has been reported in patients with intact visual and spatial perceptual ability whereas memory for landmarks is impaired (for a review, see [7,8]).

Also the neuroanatomical correlates are a matter of debate. Spatial deficits including TD have been associated with lesions due to stroke, traumatic injury, surgical treatment for epilepsy, encephalitis or neoplasia (with some exceptions, as the single case described by Iaria and colleagues [9] of a congenital brain malformation involving the bilateral retro-Rolandic regions, the case reported by Turriziani and colleagues [10] of a severe bilateral hippocampus atrophy and the

patient affected by focal Alzheimer disease recently described by Grossi and colleagues [11]). The brain regions classically involved in the different varieties of TD are the parietal lobe (generally in the right hemisphere), the dorsal occipital parietal pathway, the retrosplenial cortex, the medial temporal lobes [7,12,13]. More in detail, the contribution of the role of hippocampus in spatial processing has been emphasized by different neuropsychological studies [12–21] and confirmed by some functional neuroimaging studies [22–26].

In 1999, Aguirre and D'Esposito [1], on the basis on behavioural and neuroanatomical findings, proposed a detailed TD taxonomy considering four different categories.

Patients affected by *egocentric disorientation* are able to perceive landmarks but show difficulty in representing the location of landmarks in respect to the self (for example, [27]). Usually, the deficit is consequent to bilateral or unilateral right posterior parietal lobe lesions.

Patients with *heading disorientation* are selectively impaired with respect to the direction to go from the landmarks they are able to recognize (for example, [28]). Lesions are localized into the retrosplenial cortex–posterior cingulate (see also [29]).

A larger and well-studied group of cases with TD is that of patients affected by *landmark agnosia*, a deficit characterized by the inability to use salient environmental features for orientation [30–33]. The lesions involve cortical areas specialized in topographical representation: bilateral or right medial occipito-temporal cortex, including fusiform, lingual and parahippocampal gyri.

All the above mentioned cases of TD are impaired both in familiar and novel environments. However, some cases of TD related only to

\* Corresponding author. Department of Human Sciences, University of Bergamo, P. le S. Agostino 2, 24129 Bergamo, Italy. Tel.: +39 035 2052960; fax: +39 035 2052968.

E-mail address: [marialuisa.rusconi@unibg.it](mailto:marialuisa.rusconi@unibg.it) (M.L. Rusconi).

novel environments have been reported and have been classified by Aguirre and D'Esposito as *anterograde disorientation* [10,16,34,35]. The disturbance has mainly been attributed to a prevalent inability of learning spatial relationships by visual imagery and the critical lesion site was more frequently localized into the right hippocampus and parahippocampal areas.

As we can see, the different studies reported in literature suggest that TD is a complex multicomponent deficit and the specific role of distinct neuroanatomical areas is, in part, controversial.

In the present study, we report the case of R.G. who, when she was 22 years old, after a haemorrhagic lesion involving the right temporo-occipital region and the hippocampus, showed an impairment in memorizing environmental landmarks associated with an inability of recalling the location of different spatial landmarks, in the presence of a mild memory impairment. Furthermore, this case has provided us with the opportunity to perform a longitudinal evaluation of her clinical and neuropsychological deficits: 10 years after the stroke, the patient (who was 32 years old) revealed a persistent impairment of the ability to find the way in new environments in the context of a long-term memory deficit.

We believe our patient represents an interesting example of a long-lasting anterograde topographical amnesia with preserved remote topographical memory, in the context of a mild amnesia, also considering the extent and location of the lesion in brain areas (the right occipito-temporal region and hippocampus) involved in topographical spatial knowledge.

## 2. Case report

In 1996, R.G., a 22 year-old right-handed University student, suddenly developed an acute headache attack followed by a disturbance of consciousness. She was admitted to hospital where a CT scan revealed a right temporo-occipital haemorrhagic lesion with ventricular flooding. She underwent a ventricular-peritoneal valve derivation with consequent amelioration of vigilance state. During the year, the patient underwent neuroradiological investigations (digital angiography of cerebral vessels and Magnetic Resonance Imaging – MRI) revealing a small right arteriovenous chorioidea malformation and confirming the right occipito-temporal lesion. Therefore, a stereotaxic radiosurgery with Gamma Knife was performed. Neurological examination showed an incomplete left superior quadrantsia and deep tendon reflexes slightly asymmetrical. At the time of hospitalization, a neuropsychological examination was not performed. R.G. referred a resolution of her mild memory deficit and persistence of TD.

Three months later (1998), the patient came to our observation for the evaluation of her topographical disorders and gave informed consent to participate in the study. We submitted R.G. to a complete neuropsychological assessment and to an evaluation of different cognitive abilities involved in topographical orientation (first evaluation).

Eight years after the first evaluation (2006), persisting the topographical disturbances, the patient underwent MRI and neuropsychological examination (follow-up).

## 3. First evaluation (1998)

### 3.1. Neuroradiological examination

MRI scans performed in 1998 showed a haemorrhagic lesion in the right ventricular trigonal region with enlargement of the temporal ventricular horn (Fig. 1).

### 3.2. Neuropsychological assessment

The patient was alert and cooperative, oriented in time and place (i.e. she knew the correct date/hour and where she was).

She was submitted to a series of neuropsychological test evaluating general intelligence, attention, memory, language, calculation, executive functions and visuo-spatial abilities (see Table 1).

R.G.'s general cognitive level, by means of the WAIS-R, Wechsler Adult Intelligence Scale-Revised [36] and her scores in the other cognitive test were within normal range whereas she showed a mild impairment in the Short-story recall [37] and a deficit in the Corsi Supraspan Block Test [38].

The results confirmed the clinical impression: R.G.'s topographical deficits might be due to a memory deficit and, in particular, to a spatial learning impairment. Therefore, the patient was submitted to a more specific battery of tasks in experimental and ecological environments.

We used a situated assessment approach to highlight the patient's everyday difficulties in managing known and unknown environments.

### 3.3. Experimental evaluation

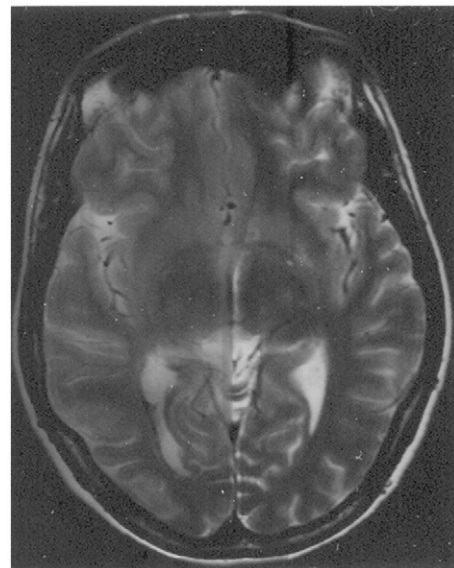
R.G.'s performance in experimental tasks is summarized in Table 2.

#### 3.3.1. Topographical abilities

**3.3.1.1. Wayfinding in familiar routes.** R.G. was asked to verbally describe, from memory, thirty-two different routes that she could take between two locations in her town, also by reporting strategies used in navigating (i.e. for some of the itineraries, she indicated a preferred route or provided an alternative route to be taken; she spontaneously described herself in a particular orientation at certain location points; she stated where a left or right turn would be made) and the location of landmarks (e.g. buildings, windows shop, cafe).

In sixteen conditions, she was asked to describe the route from her home to other familiar settings (e.g. from home to church, to bank, to supermarket etc.); in the other sixteen trials, she had to describe the route from a location to another location in her town, each with a novel starting point and a novel end-point (e.g. from the bus stop to the restaurant). The length of the routes ranged in distance from 150 to 1500 m and each itinerary included between four and ten turning points.

Her performance was balanced with the descriptions collected by her parents and friends who confirmed that the routes were well-known and frequently travelled by R.G. prior to brain damage. The



**Fig. 1.** MRI scans performed in 1998 (at the time of first evaluation) showed a haemorrhagic lesion in the right ventricular trigonal region with enlargement of the temporal ventricular horn.

**Table 1**  
Patient's performance on the tests of cognitive functions (1998)

Test	Adjusted score	Cut-off
<i>General intelligence</i>		
Wechsler Adult Intelligence Scale [36]		
Verbal IQ	119	
Performance IQ	99	
Full scale IQ	111	
Raven coloured progressive matrices [39]	34/36	18
<i>Language</i>		
Token test [38]	33/36	29
Boston Naming Test [40]	51/60	43
Phonological word fluency [37]	43	17
Semantic word fluency [37]	42	25
<i>Calculation</i>		
Acalculia test [41]	79.4/101	74
<i>Memory</i>		
Digit span [42]	5.50	3.75
Corsi span [42]	4.50	3.5
Paired words learning [37]	8.50	6.5
Short-story recall [37]	7.00 <sup>a</sup>	8
Spatial learning (Corsi Supraspan) [38]	4.25 <sup>a</sup>	6.75
Recurring faces test [43]	35.1	32.5
<i>Visuo-perceptual/visuo-spatial abilities</i>		
Poppelreuter test [44]	MF (meaningful patterns) 36/36 ML (meaningless patterns) 35/35 Total score 71/71	28 23.25 51.5
Benton line orientation test [45]	25/30	15/30
Cancellation test [46]	31/31	28/31
Street's completion test [38]	4	2
Rey's Figure copy [47]	33	23.76
<i>Digital agnosia</i>		
Finger localization [38]	24/24	14
<i>Executive and attentional functions</i>		
Tower of London Test [48]	27/36	Mean 24.9 SD 4.5
Elithorn's perceptual maze test [38]	13.25	7.75
Trial making test [49]		
A	56	<93
B	111	<282
B–A	54	<186

<sup>a</sup> Pathological value.

routes were considered to be exact if they included the correct sequence, direction and turns to reach the destination. She provided accurate descriptions of all routes, without any hesitation, thus suggesting a well-preserved retrograde spatial topographical ability. In some cases (4 out of 16), she spontaneously described a possible alternative route. For example, she reported that to get to the hairdresser shop “with the church behind my shoulders as starting point” she had to walk straight on for about 200 m, then she had to turn left at the traffic light, to go forward for 300 m, then right to the cinema (... “if I'm walking along the street... alternatively, by car, I have to go straight on, then to the right, again to the right... since it is a one-way street”), to go across a bridge “where, on the left, there is a car parking, near to the dentist's surgery” and she reached the destination point.

**3.3.1.2. Maze learning test.** This test was set up to evaluate the ability in learning eight different mazes, derived from the Wechsler Intelligence Scale for Children-Revised (WISC-R) subtest [57]. Each maze was presented for three consecutive trials with an interval of 30 s. Performance times were recorded for each of the eight mazes. R.G.'s performance was compared to that of a control group of 20 subjects, matched for age (mean=24.7, SD=1.65) and education (mean=16.15, SD=2.7).

In normal subjects, a repeated measures ANOVA showed a main effect of the time in the three consecutive trials, in all the eight mazes, demonstrating a learning effect (Maze number 1,  $F(2)=36.765, p<0.001$ ; Maze number 2,  $F(2)=13.301, p<0.001$ ; Maze number 3,  $F(2)=35.829, p<0.001$ ; Maze number 4,  $F(2)=10.851, p<0.001$ ; Maze number 5,  $F(2)=14.652, p<0.001$ ; Maze number 6,  $F(2)=25.341, p<0.001$ ; Maze number 7,  $F(2)=27.806, p<0.001$ ; Maze number 8,  $F(2)=27.806, p<0.001$ ).

The comparison between the performance of the patient and the controls (*t*-test) showed a significant difference in seven out of eight mazes (number 1→7) in which the control's group time in the first trial was higher than the patient's time but while the controls took advantage of the second and third trials, R.G.'s performance did not overall ameliorate, confirming her learning deficit (see Fig. 2).

**3.3.1.3. Road Map test.** The test consists of an A4 paper map on which a pathway is traced [50]. The patient was asked to image herself moving along that pathway and to report the left/right turns at each change of direction (for a total of 32 turns). R.G.'s score was very good (30/32) matched to the control group (mean 23, SD 2.1).

**3.3.1.4. Navigational skills in ecological environments.** Two tasks of wayfinding in unfamiliar outdoor space (*Hospital routes+route photos*) were used in order to evaluate R.G.'s ability to learn new environments. One of the task consisted in walking along nine different routes, all inside the Hospital campus (i.e. from the kiosk to the church, from the Hospital entrance to the cafe) in which the patient was accompanied by the examiner. In two subsequent steps, conversely, she was alone, followed, at distance, by the experimenter (who took detailed notes of the routes, by recording all left and right turns, her errors and hesitations). During all routes, R.G. made several direction errors, she often stopped and looked around before proceeding and seemed to be very hesitant and never sure to be right.

After the trip, some photographs of previously seen landmarks were presented to the patient who was required to put them in sequential order according to the routes she had previously followed. She was unable to do it.

**Table 2**  
Patient's performance on the experimental tests (1998)

Test	
<i>Topographical abilities</i>	
Wayfinding in familiar routes	+
Maze learning test	-
Road Map test [50]	+
Wayfinding in unfamiliar outdoor space (Hospital routes+route photos)	-
Map-based wayfinding in Hospital surroundings	+
Route-based wayfinding in Hospital surroundings	-
<i>Geographical and left-right knowledge</i>	
Italy map [38]	+
Manikin's test [51]	+
<i>Visual topographical recognition</i>	
Buildings Matching	+
Buildings Sorting	+
Famous Places recognition	+
Buildings recognition	-
<i>Visual imagery</i>	
Gordon's Questionnaire [52]	+
VVIQ [53]	+
Policardi [54]	+
Spelling	
Forward	+
Backward	+
Active/passive matrices [55,56]	+
Drawing from memory	+
“What” and “where” memorization	-

- Impaired performance; + good performance.

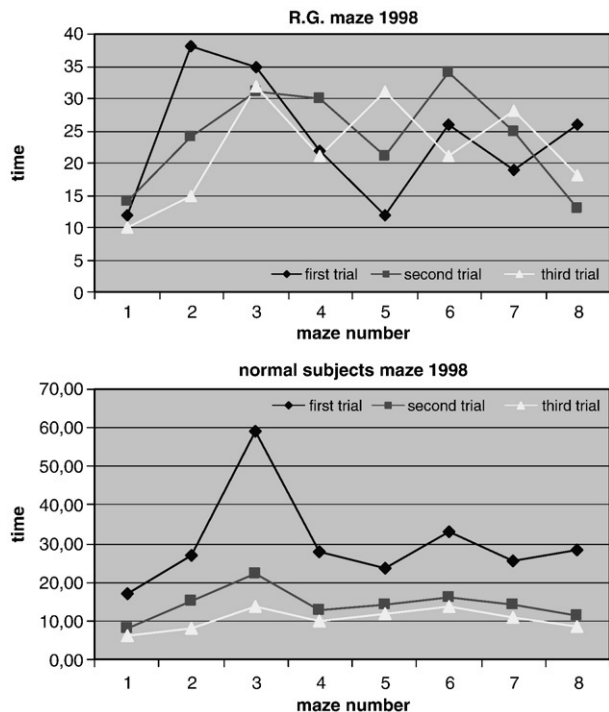


Fig. 2. Performance of the patient and the control group on the maze learning test (1998).

A second task consisted in a *Map-based wayfinding*. The patient was given a map of the Hospital surroundings on which a starting position (A) and a target position (B) were indicated. The names of the streets were cancelled (in order to avoid verbal aid) and R.G. was asked to walk from point A to point B. She performed this very well.

Then, she was requested to repeat the same route (*Route-based wayfinding*) without the aid of the map. R.G. showed a clear difficulty to perform the task, she was unable to mention the starting point (Hospital entrance) and she made various directional errors (left/right turns). Performance was scored by three independent judges on the base of accuracy.

*Comment on R.G.'s performance about topographical abilities.* The patient revealed a great difficulty in learning new spatial information, both in ecological and laboratory tasks. Topographical retrograde memory was preserved.

### 3.3.2. Geographical knowledge and left–right orientation

The abilities were assessed, respectively, by the *Italy map test* [38] and by *Manikin's test* [51].

In the first task, the patient was asked to indicate by pointing on a blank map the exact location of verbally presented Italian cities. Her performance was at a normal level (12.5/15, cut-off=7.5).

The ability to discriminate between left and right side was assessed by the second task in which the patient was requested to indicate on a manikin, drawn on a paper in 32 different rotated positions, the relevant location of left/right targets. Her score was 32/32 (control group: mean 31.15, SD 1.56).

### 3.3.3. Visual topographical recognition

The patient's ability to identify landmarks was assessed by four tests, submitted also to a control group of 20 subjects, matched for age (mean=24.7, SD=1.65) and education (mean=16.15, SD=2.7). In one test (*Buildings Matching*), the items were photographs of buildings in four different views. From the 20 items, 10 pairs of buildings were presented to R.G. who was requested to judge if the items of each pair were "same" or "different". The performance of R.G. was at normal

range matched to that of the control group (mean 19.65, SD 0.49; patient's score: 19/20;  $z=-1.32$ ). In the second test (*Buildings Sorting*), five photographs of buildings from four different views (for a total of 20) were shown to the patient who had to collect together the photographs relative to each building. Score was 20/20 (similarly to that of the control group).

In the third test (*Famous Places recognition*), twenty-six photos of famous places and monuments located in Milan ( $n=13$ ) and of other Italian cities ( $n=13$ ) were presented to the patient who was requested to recognize them and indicate which of them were in Milan (where R. G. lived likewise the normal control subjects). Score was normal (21/26,  $z=-0.76$ ; control group, mean 22.7, SD 2.1).

In the *Buildings recognition test*, three series of 20 photos of a building's front (eight targets+twelve distractors) were prepared. Eight target photos were shown to the patient: after, they were removed and represented among twelve distractors and R.G. was requested to indicate if each presented photo was previously seen (=targets) or not (=distractors). The same procedure was used for the other two series of photos, for a total of 60 items.

Patient's score (53/60), compared to that of the control group (average 58.85, SD 1.22), revealed a deficit ( $z=-4.79$ ,  $p<0.001$ ).

*Comment on R.G.'s performance about Visual topographical recognition.* R.G. showed a good performance in the above described building recognition tasks with the exception of the *Buildings recognition test* in which her defective performance could be heavily influenced by her memory deficit rather than to be referred to a "pure" recognition deficit.

### 3.3.4. Visual imagery

Visual imagery was evaluated in terms of R.G.'s ability to retrieve and describe visual characteristics of objects.

The *Gordon's Questionnaire* [52] is a visual imagery measure that examines the ability to image objects first in a canonical view (i.e. a car in a park) then in different positions which involves a mental rotation of figures or with different characteristics (i.e. colour). The ability to modify the image is rated along a 5-point scale.

*Vividness Visual Imagery Questionnaire* [53] consists of 16 items in four groups of 4 items in which the subject is invited to consider the image formed in thinking about specific scenes and situations and to define the vividness of the image. The vividness of the image is rated along a 5-point scale and has been associated with precision of outline, amount of details, brightness and saliency. Her performance to *Gordon's Questionnaire* and *Vividness Visual Imagery Questionnaire* resulted to be at normal level compared to that of a control group of 20 normal subjects, matched for age and education. The results obtained in the *Gordon's Questionnaire* were 44/50 (mean=39.25, SD=6.24, in the control group) and 65/80 in the *Vividness Visual Imagery Questionnaire* (mean=64.9, SD=9.03, in the control group).

Normal results were also obtained by our patient in tasks derived from Policardi and colleagues [54]. The tasks evaluate visual imagery in different ways (including topographical imagery, symbol imagery, animal and object imagery, and colour imagery) through comparisons of objects (patient score 20/20, controls: mean 18.9, SD 1.13), salient characteristics of objects (patient score 19/20, controls: mean 18.6, SD 1.01) and topological and metrical relations into an object (respectively, patient score 15/15, controls: mean 14.3, SD 1.18; patient score 15/15, controls: mean 14.2, SD 0.60).

Imagery of words was tested by asking to R.G. to make *spelling, forward and backward* of ten words. Her performance was perfect (10/10 correct forward and 10/10 correct backward).

The patient was also submitted to a task derived from Vecchi and colleagues [55] and Luzzatti and colleagues [56] consisting in a series of *matrices* requiring *passive* and *active* visuo-spatial processing. In the passive condition, she was presented with series of  $3 \times 3$  and  $4 \times 4$  matrices with different numbers of black squares (one, two, three targets) in perceptual and imagery conditions. In the passive perceptual task, she was requested to judge the identity of pairs of

matrices and her performance was perfect (24/24). In the passive imagery-recognition task, R.G. had to judge if the pairs of matrices presented in sequence were the same or different and she was perfectly able to perform it (24/24). In the passive imagery-recall task, a matrix was presented and after a delay of 10 s she was asked to reproduce in a blank matrix the position of the black squares. R.G.'s abilities were well preserved (23/24).

In the active condition, the patient was asked to point out a pathway of different displacement lengths (three, four, five) in a blank 4×4 square matrix in front of her by following verbal direction instructions (left-right, forward-backward). Her performance was perfect (18/18). Then, she was requested to repeat a similar task by imagining the matrix and she was asked to identify the final square. Her score was 17/18.

In *Drawing from memory* test, the patient was able to draw common objects, animals, a plan of her own apartment and the places surrounding her house maintaining scaling and spatial relationships among elements.

### 3.3.5. "What" and "where" memorization

R.G.'s ability to memorize "what" is an object and "where" it is has been verified by a new task, consisting in 40 cards representing figures of objects. All the reversed cards were presented on the table; then, the examiner disclosed one card that the patient had to observe for 5 s; after this time, the card was turned over. The patient had to count for 15 s and then she was requested to report "what" was depicted on the card she had looked at and "where" it was located. This procedure was repeated three times, also with 2, 3, 4 cards.

In two subsequent steps, the same procedure (with 1, 2, 3, 4 cards) was repeated modifying the interference task (to count for 20 s and for 25 s). We quantified the responses according the two possibility, i.e. "what" was represented on each card and "where" each card was positioned.

The task was also submitted to a control group of 14 normal subjects, matched for age (mean=24.6, SD=1.6) and education (mean=15.6, SD=1.9).

In normal subjects, a repeated measures ANOVA (Time: 15, 20, 25 s; Task: 1, 2, 3, 4 cards; response type: what/where) showed a main effect of task ( $F=29.195$ ,  $df=3.39$ ,  $p<0.001$ ), of response type ( $F=10.732$ ,  $df=1.13$ ,  $p<0.006$ ), of Task×response type ( $F=4.328$ ,  $df=3.39$ ,  $p<0.01$ ) and of Time×Task×response type ( $F=2.994$ ,  $df=6.78$ ,  $p<0.01$ ). The performance of normal subjects worsened as the number of cards increased and they revealed a better performance with "what" responses (mean=0.94) than with "where" responses (mean=0.83).

The comparison between the performance of the patient and the controls (*t*-student) showed a significant difference ( $p<0.001$ ) in 13 out of a total of 24 what/where responses. More in detail, the difference was observed with the presentation of two cards (with reference to two responses "where" and one "what"), with the presentation of three cards (with reference to three responses "where" and one "what"), with the presentation of four cards (with reference to three responses "where" and two "what"). Those results point out a significant difference between patient's and controls' performance with reference to the increase of cards number (mostly with 3 and 4 cards), and show how her performance in responses denoting the localization (where) was inferior to the "what" responses. Similarly to normal subjects, R.G.'s performance was better for "what" (mean=0.77) than for "where" (mean=0.48) responses but the number of her "where" responses was inferior to that of the control subjects.

## 4. Follow-up (2006)

Eight years after the first evaluation R.G. performed a follow-up. MRI scans confirmed the previous lesion with an involvement of the right temporo-occipital area and hippocampus (Fig. 3).

The patient referred further difficulty in orienting herself in new environments: for example, she got lost and had to ask the way out to

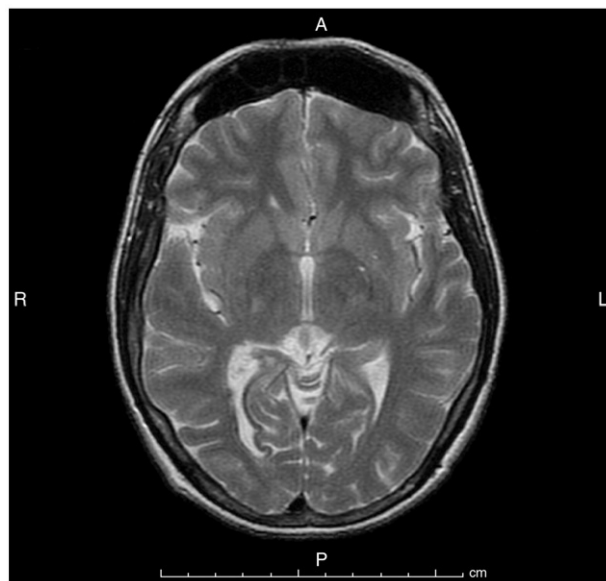


Fig. 3. MRI scans performed in 2006 (at the time of follow-up) confirmed the previous lesion: right temporo-occipital area and hippocampus.

exit from a store or restaurant she had never visited before. She referred attempts to develop wayfinding strategies for novel environments without any success. Otherwise, she referred she had no problems when leaving her apartment and walking or driving through known streets if she paid attention to some landmarks. She relied heavily, for example, on street names, shop windows, commercial signs which allowed her to locate and orient herself perfectly in familiar routes, by referring to a preserved knowledge of the map of her town. She stated: "When I go somewhere, even if I know the environments, I tell myself I'm going to pay attention... watch where I'm going, check the street names... so I feel myself more confident".

She completed university studies although some difficulties due to her memory deficits that, in the last years, became more severe and forced the patient to take note many of things regarding her daily activities.

In 2006 she was submitted to a neuropsychological and experimental follow-up.

### 4.1. Neuropsychological follow-up

The patient was cooperative and oriented in time and place. General cognitive level by WAIS and a neuropsychological battery consisting in a series of tasks similar to that of first evaluation were performed.

R.G.'s neuropsychological profile was similar to that observed in 1998 except some tasks in which she showed results below the normal level with reference to verbal and visuo-spatial long-term memory tests (Short-story recall, Rey's 15 words learning task – delayed recall, Rey's Figure – delayed recall).

The performance in neuropsychological test is summarized in Table 3.

### 4.2. Experimental follow-up

Some of the tasks used in the first examination were submitted to R.G. (summarized in Table 4).

As for as *topographical abilities*, the follow-up performance confirmed the pattern of a preserved ability of topographical retrograde memory and a difficulty to learn novel routes, both in real and in experimental condition. Tasks procedure were similar to that used for the first examination in 1998.

**Table 3**  
Patient's performance on the tests of cognitive functions (2006)

Test	Adjusted score	Cut-off
<i>General intelligence</i>		
Wechsler Adult Intelligence Scale [36]		
Verbal IQ	115	
Performance IQ	112	
Full scale IQ	118	
Raven coloured progressive matrices [39]	32.75/36	18
<i>Language</i>		
Token test [38]	32/36	29
Boston Naming Test [40]	54/60	43
Phonological word fluency [37]	55	17
Semantic word fluency [37]	50	25
<i>Calculation</i>		
Acalculia test [41]	75/101	74
<i>Memory</i>		
Digit span [42]	6.25	3.75
Corsi span [42]	4.50	3.5
Paired words learning [37]	14.50	6.5
Short-story recall [37]	2.50 <sup>a</sup>	8
Spatial learning (Corsi Supraspan) [38]	7.75	6.75
Recurring faces test [44]	35	32.5
Rey's 15 words learning task [58]		
Immediate recall	28.5	28.5
15 min delayed recall	0 <sup>a</sup>	4.7
Rey's Figure recall [47]	1.6 <sup>a</sup>	6.3
<i>Visuo-perceptual/visuo-spatial abilities</i>		
Behavioural inattention test [59]	145/146	129
Poppelreuter test [44]	MF (meaningful patterns) 36/36 ML (meaningless patterns) 35/35 Total score 71/71	29 23.25 52.5
Street's completion test [38]	3	2
Rey's Figure copy [47]	32/36	29
<i>Digital agnosia</i>		
Finger localization [38]	24/24	14
<i>Executive and attentional functions</i>		
Tower of London Test [48]	25/36	Mean 24.9 SD 4.5
Elithorn's perceptual maze test [38]	14.5	7.75
Trial making test [49]		
A	53	<93
B	134	<282
B-A	81	<186
Attentive matrices [38]	31	33

<sup>a</sup> Pathological value.

In *Wayfinding in familiar routes* task she was asked to name locations and to describe the strategies for finding some different routes in familiar settings. Her performance, compared to that of two her friends, was accurate. An interesting observation is that she provided a more detailed description of the environments she learned to know prior to her lesion which were well-practised and frequently experienced than of known places more recently acquired and experienced (within 5–6 years earlier). For the former ones, she reported also elements such as houses, shops, parks and so on whereas for the latter ones she provided a correct but more schematic topographical map describing only those elements which represent valid cues for navigation.

In *Wayfinding in unfamiliar outdoor space* task, R.G. was invited to walk along unfamiliar routes with and without the aid of a map (*Map-based wayfinding and route-based wayfinding*), with the only difference (respect to the evaluation performed in 1998) that the location was not the same Hospital in which R.G. was hospitalized in 1998. R.G.'s performance was scored by two independent judges on the base of accuracy and resulted to be very compromised. She made

errors about left/right turns, she expressed difficulty in knowing where she was in the space with evident hesitations about the exact location.

The *Road Map test* was submitted to a control group of 12 subjects matched for age (mean=30.08, SD=2.9) and education (mean=17.5, SD=0.52). R.G.'s score was normal (32/32) matched to the controls (mean 22, SD 2.3).

R.G.'s performance on the *maze test* was compared to that of a control group, matched for age (mean=30.1, DS 2.9) and education (mean=17.4, DS 0.5). In normal subjects, repeated ANOVA measures showed a main effect in the time needed to complete the test in the three consecutive trials, in 7 out of 8 mazes, demonstrating a learning effect (Maze number 1,  $F(2)=13.937$ ,  $p<0.002$ ; Maze number 2,  $F(2)=3.6$ ,  $p$ =not significant; Maze number 3,  $F(2)=7.736$ ,  $p<0.01$ ; Maze number 4,  $F(2)=8.663$ ,  $p<0.01$ ; Maze number 5,  $F(2)=18.687$ ,  $p<0.001$ ; Maze number 6,  $F(2)=7.828$ ,  $p<0.01$ ; Maze number 7,  $F(2)=10.714$ ,  $p<0.005$ ; Maze number 8,  $F(2)=4.661$ ,  $p<0.004$ ).

The comparison between the performance of the patient and the controls ( $t$ -test) revealed a significant difference in four out of eight mazes (mazes number 3–4–5–7). The control group showed a clear learning effect across the trials while R.G.'s performance showed a remarkable difference with the normal subjects' values in all experimental conditions. She was significantly slower than the normal controls with a peculiar peak in the second trial of the Maze number 3 confirming her attentive and memory impairment (see Fig. 4).

*Geographical knowledge* was evaluated through the *Italy map test* and it resulted to be at a normal level (12/15, cut-off=7.5).

*Left–right orientation ability* (Manikin's test, R.G.'s score 30/32, control group: mean 31, SD 1.6) and *Visual imagery* test (spelling forward/backward and Drawing from memory) were well performed.

In *Visual topographical recognition tasks*, R.G.'s score compared to the control group confirmed a good performance in three tests: *Buildings Matching* (score=19/20,  $z=-1.2$ ) *Buildings Sorting* (score=20/20), *Famous Places* (score=24/26,  $z=0.8$ ).

In the *Buildings recognition test*, she showed a mild impairment (score=54/60,  $z=-2.5$ ,  $p<0.001$ ).

*"What" and "where" memorization task*: in normal subjects, a repeated measures ANOVA (Time: 15, 20, 25 s; Task: 1, 2, 3, 4 cards; response type: what/where) showed a main effect of task ( $F=71.455$ ,

**Table 4**  
Patient's performance on the experimental tests (2006)

Test	
<i>Topographical abilities</i>	
Wayfinding in familiar routes	+
Maze learning test	-
Road Map test [50]	+
Wayfinding in unfamiliar outdoor space	-
Map-based wayfinding	+
Route-based wayfinding	-
<i>Geographical and left–right knowledge</i>	
Italy map [38]	+
Manikin's test [51]	+
<i>Visual topographical recognition</i>	
Buildings Matching	+
Buildings Sorting	+
Famous Places recognition	+
Buildings recognition	-
<i>Visual imagery</i>	
Spelling	
Forward	+
Backward	+
Drawing from memory	+
"What" and "where" memorization	-

- Impaired performance; + good performance.

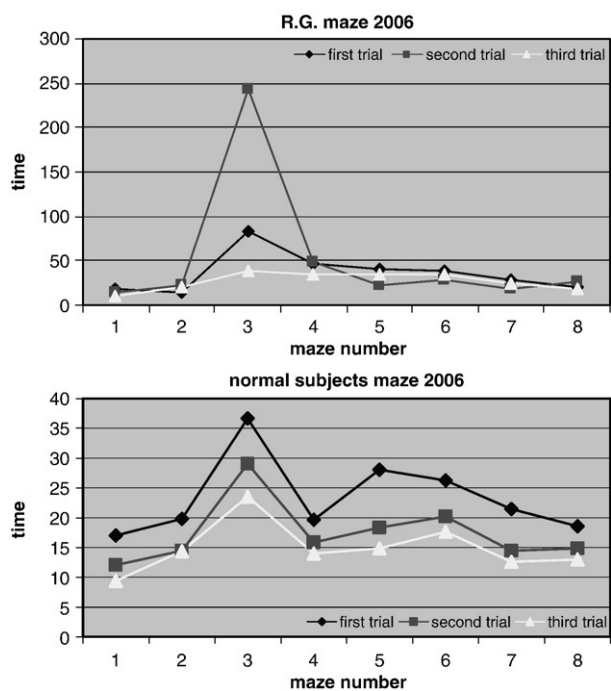


Fig. 4. Performance of the patient and the control group on the maze learning test (2006).

$df=3$ ,  $p<0.000$ ) and of Task $\times$ response type ( $F=5.582$ ,  $df=6$ ,  $p<0.028$ ). The performance of normal subjects worsened as the number cards increased and they revealed a better performance with “what” responses (mean=0.88) than with “where” responses (mean=0.84).

The comparison between the performance of the patient and the controls ( $t$ -student) showed a significant difference ( $p<0.001$ ) in 9 responses out of a total of 24 what/where responses. More specifically, the difference was observed with the presentation of two cards (with reference to two responses “where” and one “what”), with the presentation of three cards (with reference to two responses “where” and one “what”), with the presentation of four cards (with reference to two responses “where” and one “what”). Similarly to normal subjects, R.G.’s performance was better for “what” (mean=0.79) than for “where” responses (mean=0.66) but the number of her “where” responses was inferior to that of the control subjects.

*Comment on R.G.’s performance about experimental tasks* R.G.’s performance in 2006 resulted to be similar to that observed in 1998. The patient revealed a great difficulty in learning new spatial information, both in ecological and laboratory tasks, with a more evident attentive difficulty in performing some tasks (for example, the maze test). Topographical retrograde memory, visual perceptual and imagery abilities were preserved.

## 5. Discussion

We have described the case of a patient who showed a severe and long-lasting impairment in orienting herself in novel environments after a haemorrhagic lesion of the right temporo-occipital region including the hippocampus. The deficit in spatial learning was evident both in neuropsychological and experimental conditions, whereas the ability to recall and navigate through known routes was preserved, as well as her capacity to recognize familiar buildings and landscapes.

As reported in the Introduction, few cases of TD resulted to be restricted to anterograde memory deficits [10,16,34,35]. Usually, TD is observed in brain-damaged patients who are not able to recall previously known routes and to learn new routes (see [1] for a review). Selective TD is rare and it has classically been divided into

two distinct forms, considering a different basic impairment of perceptive or mnemonic nature: topographical amnesia and topographical agnosia. Topographical agnosia is defined as a type of visual perceptive failure to recognize the characteristic features of landmarks (places or buildings). Topographical amnesia is observed with reference to memory deficits and can be divided into two subtypes: amnesia for landmarks and amnesia for spatial relationships. The former (see, for example, [33]) is characterized by a preserved ability in recognizing visual landmarks useful for real-world wayfinding (for example, street names and store signs) with an evident difficulty in recalling. In the latter case, patients are unable to recall the spatial location of different landmarks related to each other (for example, [2,35]).

The present case shows a patient with a difficulty in learning the spatial relationships both in real-world and laboratory wayfinding tests. R.G.’s clinical evaluation and neuropsychological testing revealed a similar pattern of TD at the time of the first and of the follow-up examination despite the fact that her memory impairment resulted to be slightly different. On the neuropsychological evaluation performed in 1998, our patient showed a mild deficit in one test of verbal long-term memory (Short-story recall) and a deficit in one test of visuo-spatial long-term memory (Corsi Supraspan Block). Other cognitive functions resulted to be unaffected. Eight years later (2006), she showed a deficit with reference to verbal and visuo-spatial long-term memory tests (Short-story recall, Rey’s 15 words learning task – delayed recall, Rey’s Figure – delayed recall), confirming her personal and our clinical impression of a slight worsening of attentive and memory functions, in the context of a good preservation of general cognitive functions.

The analysis of our patient’s performance in some experimental tasks can be particularly helpful in understanding the nature of her TD.

A possible impact of visuo-perceptual deficits on TD can be ruled out by the observation that the performance on experimental evaluation was at a normal level in the visual recognition tasks (buildings, famous places, monuments).

On the other hand, the deficit reported in the Building recognition test, in which she had to recognize photographs of previously seen buildings, could be suggestive for a mild amnesia for landmarks rather than for a pure perceptual deficit.

Our patient showed a clear dissociation between a preserved capacity to describe and follow familiar routes and a severe impairment of wayfinding abilities in an unknown environment, both in real (Hospital routes and surroundings test) and laboratory conditions (maze test). Interestingly, the use of visuo-perceptive informations (a map) improved R.G.’s ability to follow a route in a real setting. In familiar wayfinding tasks, she was able to describe different locations by relying on a well-preserved mental representation of the environment, a “cognitive map” which allowed her to move from one place to another by following a known route. Even if we did not systematically investigate her ability to find an alternative route assuming that one main street was blocked off [21,26] we may reasonably presume that such ability, in some routes, was preserved since she spontaneously referred an alternative route in her descriptions (see the example in the experimental evaluation).

However, from a methodological point of view, it is necessary to highlight a common problem in many studies: it is not easy to validate subjects’ reports of remote spatial memory. As suggested by Spiers and Maguire, 2007, page 8 [60]: “Arguably the most intuitive and indeed ecologically valid way to probe remote spatial memory is to concentrate on knowledge acquired of real-world places and environments learned in the past... Thus, it is important to consider how such tasks are being performed by subjects...”.

Therefore, stated the difficulty to have a control group, the descriptions made by our patient, by memory or in real settings, were recorded and balanced by independent judges.

Considering R.G.'s performance in the different tasks, we think that her TD can be referred to an impairment in learning spatial informations. One of the main finding is that she was unable to follow novel routes despite a good recognition of some landmarks along the way. For example, she was capable of recognizing photographs of previously seen landmarks along a way but she showed a severe difficulty in putting those photographs in order to reproduce the followed route. To assess the distinction between “what” is an object and “where” is it, we developed a visuo-spatial recognition test (“what” and “where” memorization). Once again in favour of our interpretation of R.G.'s topographical deficit, the results obtained by our patient, who showed a better performance with “what” responses, could be related to her difficulty in memorizing the spatial relationships.

However, it is to note that her quantitative performance in this test was slightly different in 1998 and in 2006, although with a similar pattern. This could be referred to a more general worsening observed, at the follow-up, in the above mentioned three tests of verbal and visuo-spatial long-term memory. This is consistent with R.G.'s report that, 10 years after the stroke, her subjective attentive and memory deficits had worsened her daily life. She was independent in most of the common daily activities but she had to use some strategies to memorize different information, in the context of a persistent TD in unfamiliar environments.

It is unlikely that R.G.'s TD could be primarily referred to as an imagery impairment since she performed all tasks very well.

In the previously reported cases of patients with anterograde TD in the absence of a long-lasting retrograde TD, the role of the medial temporal region has been highlighted with a prevalent involvement of the right hemisphere [16,34,61,62,63]. More recently, different studies of topographical learning have pointed out the involvement of a more diffuse network of cortical and subcortical areas. For example, the results obtained by Barrash and colleagues [12] underlined, in a large sample of brain-damaged patients, the relevance of medial occipito-temporal cortices (bilaterally), the right infero-temporal cortex, the right hippocampus and parahippocampal gyrus in the learning of a complex real-life route. More in detail, the role of the right hippocampus and parahippocampus is still a matter of debate: according to the Authors, those regions are crucially involved in the consolidation of the topographical representation by integrating informations about landmarks and their locations (see also [64]). The relevant role of the hippocampus in the formation and use of cognitive maps in humans has been established by different neuropsychological [12–21] and functional neuroimaging studies [22–26]. Some recent studies of anterograde and retrograde amnesia after hippocampal lesions have focused on the processes and neuroanatomical correlates implicated in remote spatial memory (for a review, see [60]). Three different theories (cognitive map theory [65], standard consolidation theory [66] and multiple trace theory [67,68]) may account for the involvement of the hippocampus and the medial temporal lobes in the acquisition and retrieval of spatial memory. Despite different aspects among these three theories, it seems clear the hippocampus is particularly necessary for facilitating navigation using detailed spatial representations [69], whereas the role of a more diffuse neural network, including parahippocampus, retrosplenial and parietal cortices, is still a matter of debate.

Our patient showed a clear dissociation between preserved retrograde topographical memory and impaired anterograde topographical memory, in the context of a mild amnesia. Her description of experienced environments can be considered as “relatively” detailed. She retained egocentric and allocentric spatial memory for maps of the environments and reported landmarks crucial for navigation but only in few cases she provided a more detailed description. Interestingly, at the follow-up, she revealed slight different qualitative descriptions of recollective experiences with respect to age of memories for places she had learned to know prior to her lesion.

These clinical observations, together with the hippocampal lesion, seem to be consistent with the multiple trace theory [68], which posits that the hippocampus is necessary for detailed representations of remote memory (episodic) but not for schematic, remote topographical memory, sufficient for navigation (semantic).

The location of lesion together with other clinical and experimental findings allows us to underline that our patient differs, in some aspects, from other interesting patients reported into literature, such as patients E.P. [21], K.C. [70], S.B. [71], T.T. [69].

R.G. did not show a bilateral lesion or diffuse atrophy involving the hippocampus and/or parahippocampus. She has a unilateral right temporo-occipital lesion, also including but not exclusively limited to the hippocampus.

R.G. showed a mild amnesia but a severe anterograde TD while the other patients were severe amnesic or with a probable Alzheimer's disease (S.B.).

Patients E.P., K.C. and S.B. were studied with static tests while we used also ecological tasks and had the opportunity to follow-up our patient. However, R.G. can probably not be compared with T.T., a London taxi driver, with a preserved retrograde topographical memory but an impairment on a task involving active navigation in London, evaluating with an interactive virtual reality London taxi.

We have to acknowledge that we tested R.G. using environments that have a relatively less complex layout (compared to Toronto and, specially, to London). It might be that in such environments the role of the hippocampus in R.G.'s performance was minimized (see [72] and [73]).

From a clinical and neuropsychological point of view, our patient is similar to the one described by Turriziani and colleagues [10] whereas the neural correlates are very different. Their patient showed a severe deficit in orienting himself in new environments in the context of a mild global amnesic syndrome following a bilateral hippocampal atrophy and represents an example of the involvement of hippocampus in the acquisition of new topographical spatial knowledge. R.G. showed a right medial temporo-occipital lesion including the hippocampus that could account for her topographical disorders and for her mild verbal and visuo-spatial memory deficits (particularly at the follow-up time).

TD may also be distinguished [74] between a form caused by the impairment of “visual-object” (landmark) representations, subtended by the “what” visual system (the ventral pathway passing through temporo-occipital regions) and a form caused by the impairment of “visuo-spatial” representations, subtended by the “where” visual system (the dorsal pathway passing through parietal region) [75]. This separation between neural correlates with regard to the identification of objects and the localization of objects was criticized by Milner and Goodale [76] and by Farrell [8] sustaining that both components (“what” and “where”) may be processed by both dorsal and ventral visual pathway although with different purposes. The ventral stream would be involved in perception and identification of spatial informations “allocentrically”; the dorsal stream would be encode spatial informations “egocentrically” for the guidance of actions directed at objects in the world (see also [77]). On the other hand, Aguirre and D'Esposito [1] claimed the difficulty to consider a unique neural correlate that could subserve both the identification of landmarks and their relative positions.

As we can see, there is not a wide agreement in literature with regard to the neuroanatomical correlates involved in processing the functional dissociation between landmark information and position information, although the hippocampus seems to be critically relevant in associating objects and their locations. In our study, damage to the right ventral stream temporo-occipital cortex (and hippocampus) did not result in impaired landmark recognition. R.G. was able to recognize visual landmarks but she was unable to locate and to use them for navigation in new environments. This possible dissociation between “what” and “where” aspects of visual processing was also evaluated and confirmed by a new object-location memory test



(“what” and “where” memorization task) in which she performed worse with “where” than with “what” items, findings that might be critically considered in the light of recent observations (for a review, see [78]).

In conclusion, TD is not a unitary deficit but clearly involves a variety of cognitive processes and distinct brain areas. As such, we believe the current study might also contribute to the debate on the role of neural correlates in the acquisition of new topographical spatial knowledge.

## Acknowledgements

The authors would like to thank Stefano Zago and Chiara Scarabelli for their help in a preliminary data collection and the anonymous reviewer for the helpful comments and suggestions.

## References

- [1] Aguirre GK, D'Esposito M. Topographical disorientation: a synthesis and taxonomy. *Brain* 1999;122:1613–28.
- [2] Bottini G, Cappa S, Geminiani G, Sterzi R. Topographic disorientation – a case report. *Neuropsychologia* 1990;28:309–12.
- [3] De Renzi E. Disorders of space exploration and cognition. Chichester: Wiley; 1982.
- [4] Landis T, Cummings JL, Benson DF, Palmer EP. Loss of topographic familiarity: an environmental agnosia. *Arch Neurol* 1986;43:132–6.
- [5] Paterson A, Zangwill OL. A case of topographical disorientation associated with a unilateral cerebral lesion. *Brain* 1945;68:188–212.
- [6] Rainville C, Joubert S, Feliciano O, Chabanne V, Ceccaldi M, Péruch P. Wayfinding in familiar and unfamiliar environments in a case of progressive topographical agnosia. *Neurocase* 2005;11:297–309.
- [7] Barrash J. A historical review of topographical disorientation and its neuroanatomical correlates. *J Clin Exp Neuropsychol* 1998;20:807–27.
- [8] Farrell MJ. Topographical disorientation. *Neurocase* 1996;2:509–20.
- [9] Iaria G, Inccoccia C, Piccardi L, Nico D, Sabatini U, Guariglia C. Lack of orientation due to a congenital brain malformation: a case study. *Neurocase* 2005;11:463–74.
- [10] Turriziani P, Carlesimo GA, Perri R, Tomaiuolo F, Caltagirone C. Loss of spatial learning in a patient with topographical disorientation in new environments. *J Neurol Neurosurg Psychiatry* 2003;74:61–9.
- [11] Grossi D, Fasanaro A, Cecere R, Salzano S, Trojano L. Progressive topographical disorientation: a case of focal Alzheimer's disease. *Neurol Sci* 2007;2:107–10.
- [12] Barrash J, Damasio H, Adolphs R, Tranel D. The neuroanatomical correlates of route learning impairment. *Neuropsychologia* 2000;38:820–36.
- [13] Maguire EA. The retrosplenial contribution to human navigation: a review of lesion and neuroimaging findings. *Scand J Psychol* 2001;42(3):225–38.
- [14] Bird CM, Shallice T, Cipolotti L. Fractionation of memory in medial temporal lobe amnesia. *Neuropsychologia* 2007;45:1160–71.
- [15] Cipolotti L, Bird C, Good T, Macmanus D, Rudge P, Shallice T. Recollection and familiarity in dense hippocampal amnesia: a case study. *Neuropsychologia* 2006;44:489–506.
- [16] Habib M, Sirigu A. Pure topographical disorientation: a definition and anatomical basis. *Cortex* 1987;23:73–85.
- [17] Maguire EA, Burke T, Phillips J, Staunton H. Topographical disorientation following unilateral temporal lobe lesions in humans. *Neuropsychologia* 1996;34:993–1001.
- [18] Smith ML, Milner B. The role of the right hippocampus in the recall of spatial location. *Neuropsychologia* 1981;19:781–93.
- [19] Smith ML, Milner B. Right hippocampal impairment in the recall of spatial location: encoding deficit or rapid forgetting. *Neuropsychologia* 1989;27:71–81.
- [20] Squire LR, Zola-Morgan S. Memory: brain systems and behaviour. *Trends Neurosci* 1988;11:170–5.
- [21] Teng E, Squire LR. Memory for places learned long ago is intact after hippocampal damage. *Nature* 1999;400:675–7.
- [22] Hartley T, Maguire EA, Spiers HJ, Burgess N. The well-worn route and the path less traveled: distinct neural bases of route following and wayfinding in humans. *Neuron* 2003;37:877–88.
- [23] Iaria G, Petrides M, Dagher A, Pike B, Bohbot VD. Cognitive strategies dependent on the hippocampus and caudate nucleus in human navigation: variability and change with practice. *J Neurosci* 2003;23:5945–52.
- [24] Maguire EA. Hippocampal involvement in human topographical memory: evidence from functional imaging. *Philos Trans R Soc Lond B* 1997;352:1475–80.
- [25] Maguire EA, Burgess N, Donnett JG, Frackowiak RS, Frith CD, O'Keefe J. Knowing where and getting there: a human navigation network. *Science* 1998;280:921–4.
- [26] Maguire EA, Frackowiak RS, Frith CD. Recalling routes around London: activation of the right hippocampus in taxi drivers. *J Neurosci* 1997;17:7103–10.
- [27] Stark M, Coslett HB, Saffran EM. Impairments of an egocentric map of locations: implications for perception and action. *Cogn Neuropsychol* 1996;13:481–523.
- [28] Takahashi N, Kawamura M, Shiota J, Kasahata N, Hirayama K. Pure topographic disorientation due to right retrosplenial lesion. *Neurology* 1997;49:464–9.
- [29] Cammalleri R, Gangitano M, D'Amelio M, Raieli V, Raimondo D, Camarda R. Transient topographical and cingulate cortex damage: a case report. *Neuropsychologia* 1996;34:321–6.
- [30] Hécaen H, Tzortzis C, Rondot P. Loss of topographic memory with learning deficits. *Cortex* 1980;16:525–42.
- [31] Incisa della Rocchetta A, Cipolotti L, Warrington EK. Topographical disorientation: selective impairment of locomotor space? *Cortex* 1996;32:727–35.
- [32] Pallis CA. Impaired identification of faces and places with agnosia for colours. *J Neurol Neurosurg Psychiatry* 1955;18:218–24.
- [33] Whiteley AM, Warrington EK. Selective impairment of topographic memory: a single case study. *J Neurol Neurosurg Psychiatry* 1978;41:575–8.
- [34] Epstein R, De Yoe EA, Press DZ, Rosen AC, Kanwisher N. Neuropsychological evidence for a topographical learning mechanism in parahippocampal cortex. *Cogn Neuropsychol* 2001;18:481–508.
- [35] Luzzi S, Pucci E, Di Bella P, Piccirilli M. Topographical disorientation consequent to amnesia of spatial location in a patient with parahippocampal damage. *Cortex* 2000;36:427–34.
- [36] Wechsler D. Manual for the Wechsler Adult Intelligence Scale-Revised (WAIS-R). San Antonio, TX: Psychological Corporation; 1981.
- [37] Novelli G, Papagno C, Capitani E, Laiacona M, Vallar G, Cappa SF. Tre test clinici di memoria verbale a lungo termine. Taratura su soggetti normali. *Arch Psicol Neurol Psichiatr* 1986;47:278–96.
- [38] Spinnler H, Tognoni G. Standardizzazione e Taratura Italiana di Test Neuropsicologici. *Ital J Neurol Sci* 1987;8(6).
- [39] Measso G, Zappalà G, Cavarzeran F, Crook TH, Romani L, Pirozzolo FJ, et al. Raven's coloured progressive matrices: a normative study on a random sample of healthy adults. *Acta Neurol Scand* 1993;88:70–4.
- [40] Kaplan E, Goodglass H, Weintraub S. The Boston Naming Test. Philadelphia: Lea & Febiger, 1978, 1983.
- [41] Basso A, Capitani E. Un test standardizzato per la diagnosi di acalculia: descrizione e valori normativi. *Riv Appl Psicol* 1979;1(3):551–64.
- [42] Orsini A, Grossi D, Capitani E, Laiacona M, Papagno C, Vallar G. Verbal and spatial immediate memory span: normative data from 1355 adults and 1112 children. *Ital J Neurol Sci* 1987;8:539–48.
- [43] Bertolani L, De Renzi E, Faglioni P. Test di memoria non verbale di impiego diagnostico in clinica: taratura su soggetti normali. *Arch Psicol Neurol Psichiatr* 1993;54:477–86.
- [44] Della Sala S, Laiacona M, Trivelli C, Spinnler H. Poppelreuter–Ghent's overlapping figures test: its sensitivity to age, and its clinical use. *Arch Clin Neuropsychol* 1995;10:511–34.
- [45] Benton AL, Varney NR, des Hamsher K. Visuospatial judgment: a clinical test. *Arch Neurol* 1978;35:364–7.
- [46] Vallar G, Rusconi ML, Fontana F, Musicco M. Tre test di esplorazione visuo-spaziale: taratura su 212 soggetti normali. *Arch Psicol Neurol Psichiatr* 1994;4:827–41.
- [47] Carlesimo G, Buccione I, Fadda L, Graceffa A, Mauri M, Lo Russo S, et al. Standardizzazione di due test di memoria per uso clinico: Breve Racconto e Figura di Rey. *Riv Neurol* 2002;12:1–13.
- [48] Shallice T. Specific impairments of planning. *Philos Trans R Soc London B* 1982;298:199–209.
- [49] Giovagnoli AR, Del Pesce M, Mascheroni S, Simoncelli M, Laiacona M, Capitani E. Trail making test: normative values from 287 normal adult controls. *Ital J Neurol Sci* 1996;17:305–9.
- [50] Money J, Alexander D, Walker HT. A Standardized Road-Map Test of Direction Sense. Baltimore: Johns Hopkins Press; 1967.
- [51] Ratcliff G. Spatial thought, mental rotation and the right cerebral hemisphere. *Neuropsychologia* 1979;17:49–54.
- [52] Gordon R. An investigation into some of the factors that favour the information of stereotypic images. *Br J Psychol* 1949;39:156–67.
- [53] Marks DF. Visual imagery differences in the recall of pictures. *Br J Psychol* 1973;64:17–24.
- [54] Policardi E, Perani D, Zago S, Grassi F, Fazio F, Ladavas E. Failure to evoke visual imagery in a patient with cortical blindness. *Neurocase* 1996;2:265–83.
- [55] Vecchi T, Ponticelli ML, Cornoldi C. Visuo-spatial working memory: structures and variables affecting a capacity measure. *Neuropsychologia* 1995;33:1549–64.
- [56] Luzzatti C, Vecchi T, Agazzi D, Cesa-Bianchi M, Vergani C. A neurological dissociation between preserved visual and impaired spatial processing in mental imagery. *Cortex* 1998;34:461–9.
- [57] Wechsler D. Manual for the Wechsler Intelligence Scale for Children-Revised (WISC-R). San Antonio, TX: Psychological Corporation; 1974.
- [58] Carlesimo GA, Caltagirone C, Gainotti G. The group for the standardization of the mental deterioration battery. The mental deterioration battery: normative data, diagnostic reliability and qualitative analyses of cognitive impairment. *Eur Neurol* 1996;36(6):378–84.
- [59] Wilson B, Cockburn J, Halligan PW. The Behavioural Inattention Test. Bury St. Edmunds, UK: Thames Valley Test Company; 1987.
- [60] Spiers HJ, Maguire EA. The neuroscience of remote spatial memory: a tale of two cities. *Neuroscience* 2007;149:7–27.
- [61] De Renzi E, Faglioni P, Villa P. Topographical amnesia. *J Neurol Neurosurg Psychiatry* 1977;40:498–505.
- [62] Ross ED. Sensory-specific and fractional disorders of recent memory in man. Isolated loss of visual recent memory. *Arch Neurol* 1980;37:193–200.
- [63] Scotti G. La perdita della memoria topografica: descrizione di un caso. *Sist Nerv* 1968;20:352–61.
- [64] Bohbot V D, Kalina M, Stepankova K, Spackova N, Petrides M, Nadel L. Spatial memory deficits in patients with lesions to the right hippocampus and to the right parahippocampal cortex. *Neuropsychologia* 1998;36:1217–38.
- [65] O'Keefe J, Dostrovsky J. The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. *Brain Res* 1971;34:171–5.

- [66] Squire LR, Alvarez P. Retrograde amnesia and memory consolidation: a neurobiological perspective. *Curr Opin Neurobiol* 1995;5:169–77.
- [67] Moscovitch M, Rosenbaum RS, Gilboa A, Addis DR, Westmacott R, Grady C, et al. Functional neuroanatomy of remote episodic and semantic and spatial memory: a unified account based on multiple trace theory. *J Anat* 2005;207:35–66.
- [68] Moscovitch M, Nadel L, Winocur G, Gilboa A, Rosenbaum RS. The cognitive neuroscience of remote episodic and semantic and spatial memory. *Curr Opin Neurobiol* 2006;16:179–90.
- [69] Maguire EA, Nannery R, Spiers HJ. Navigation around London by a taxi driver with bilateral hippocampal lesions. *Brain* 2006;19:2894–907.
- [70] Rosenbaum RS, Priselac S, Kohler S, Black SE, Gao F, Nadel L, et al. Remote spatial memory in an amnesic person with extensive bilateral hippocampal lesions. *Nat Neurosci* 2000;3:1044–8.
- [71] Rosenbaum RS, Kohler S, Schacter DL, Moscovitch M, Westmacott R, Black SE, et al. The case of K.C.: contributions of a memory-impaired person to memory theory. *Neuropsychologia* 2005;43:989–1021.
- [72] Rosenbaum RS, Ziegler M, Winocur G, Grady CL, Moscovitch M. I have often walked down this street before”: fMRI studies on the hippocampus and other structures during mental navigation of an old environment. *Hippocampus* 2004;14:826–35.
- [73] Spiers HJ, Maguire EA. Thoughts, behavior and brain dynamics during navigation in the real world. *Neuroimage* 2006;31:1826–40.
- [74] Levine DN, Warach J, Farah M. Two visual systems in mental imagery: dissociation of “what” and “where” in imagery disorders due to bilateral posterior cerebral lesions. *Neurology* 1985;35:1010–8.
- [75] Ungerleider LG, Mishkin M. Two cortical visual systems. In: Ingle DJ, Goodale MA, Mansfield RJW, editors. *Analysis of visual behaviour*. Cambridge, MA: MIT Press; 1982. p. 549–86.
- [76] Milner AD, Goodale MA. *The visual brain in action*. Oxford: Oxford University Press; 1995.
- [77] Milner AD, Goodale MA. Two visual systems re-viewed. *Neuropsychologia* 2008;46:774–85.
- [78] A. Postma, R.P.C. Kessels, M. van Asselen. How the brain remembers and forgets where things are: the neurocognition of object location memory. *Neurosci Biobehav Rev*, doi:10.1016/j.neubiorev.2008.05.001.