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Hurt but still alive: Residual activity in the parahippocampal cortex conditions the recognition of familiar places in a patient with topographic agnosia☆

Mitsouko van Assche[a,b,*], Valeria Kebets[a,b], Ursula Lopez[b,c], Arnaud Saj[a,b], Rachel Goldstein[a,b], Françoise Bernasconi[b,c], Patrik Vuilleumier[a], Frédéric Assal[a,b]

[a]Faculty of Medicine, University of Geneva, Geneva, Switzerland
[b]Department of Neurology, Geneva University Hospitals, Geneva, Switzerland
[c]Faculty of Psychology, University of Geneva, Geneva, Switzerland

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ABSTRACT

The parahippocampal cortex (PHC) participates in both perception and memory. However, the way perceptual and memory processes cooperate when we navigate in our everyday life environment remains poorly understood. We studied a stroke patient presenting a brain lesion in the right PHC, which resulted in a mild and quantifiable topographic agnosia, and allowed us to investigate the role of this structure in overt place recognition. Photographs of personally familiar and unfamiliar places were displayed during functional magnetic resonance imaging (fMRI). Familiar places were either recognized or unrecognized by the patient and 6 age- and education-matched controls in a visual post-scan recognition test. In fMRI, recognized places were associated with a network comprising the fusiform gyrus in the intact side, but also the right anterior PHC, which included the lesion site. Moreover, this right PHC showed increased connectivity with the left homologous PHC in the intact hemisphere. By contrasting recognized with unrecognized familiar places, we replicate the finding of the joint involvement of the retrosplenial cortex, occipito-temporal areas, and posterior parietal cortex in place recognition. This study shows that the ability for left and right anterior PHC to communicate despite the neurological damage conditioned place recognition success in this patient. It further highlights a hemispheric asymmetry in this process, by showing the fundamental role of the right PHC in topographic agnosia.

1. Introduction

Neuroimaging studies in healthy participants have pointed out the specificity of the region of the posterior parahippocampal cortex (PHC), since the discovery of its high sensitivity to places and buildings as opposed to other stimulus categories (Aguirre et al., 1998; Epstein and Kanwisher, 1998). This place-sensitive area supports the coding of the spatial layout of scenes, a necessary step before their encoding and later recognition (review in Epstein, 2008), and a challenging task given the number of places that we cross every day. A related function is the coding of objects-place associations, particularly on the right hemisphere (Owen et al., 1996). However, the contribution of PHC to the visual recognition process itself remains unclear (Sewards, 2011; Spiers and Maguire, 2007), since previous neuroimaging studies yielded mixed findings in neurologically healthy participants (Epstein, 2008; Epstein et al., 2007), see also (Epstein and Higgins, 2007) and supported a clearer role of the retrosplenial complex (RSC) in this function (Epstein, 2008; Spiers and Maguire, 2007; Sugiura et al., 2005). Thus, it is uncertain to which extent the PHC is implicated during place recognition, beyond its role in perceptual processing.

More insights may be gained with the study of brain-lesioned patients, by determining whether a target area is necessarily required for place analysis, or whether this function can be shouldered by a any other brain region. Topographic agnosia or disorientation is a neurological condition in which patients become unable to find their way in the environment following a focal brain damage (Aguirre and D'Esposito, 1999; De Renzi, 1982). In a specific form of this disorder called landmark agnosia (Aguirre and D'Esposito, 1999), a lesion around the right posterior PHC — the region of the right anterior lingual gyrus/PHC/medial fusiform gyrus — usually impairs spatial orientation in familiar environments, but spares the ability to describe them (e.g. Busigny et al., 2014; Habib and Sirigu, 1987; Landis et al., 1986; Takahashi and Kawamura, 2002). This condition arises as a failure to recognize typical landmarks known before the lesion occurrence (Incisa della Rocchetta et al., 1996; Landis et al., 1986; Pallis, 1955; Rainville et al., 2005; Whiteley

☆ Place recognition in topographic agnosia.

* Corresponding author at: Department of Neurology, Geneva University Hospital, rue Gabrielle-Perret-Gentil 4, 1211, Geneva, Switzerland.
E-mail address: mitsouko.vanassche@unige.ch (M. van Assche).

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and Warrington, 1978), disrupting the interaction between perceptual and memory processes (Brunsdon et al., 2007). However, the specific study of the relationships between landmark agnosia, place familiarity, and the location of the lesion in patients with peri-hippocampal lesions has yielded mixed findings, with patients either showing preserved (Habib and Sirigu, 1987; Takahashi and Kawamura, 2002) or altered recognition of known places (Habib and Sirigu, 1987; Hecaen et al., 1980; Incisa della Rocchetta et al., 1996; Pallis, 1955; McCarthy et al., 1996; Takahashi and Kawamura, 2002; Whiteley and Warrington, 1978). A common feature of patients with preserved topographic abilities in familiar environments is the sparing of visual areas located posterior to the PHC (review in Sewards, 2011). On the other hand, disconnection following a focal lesion of the PHC may play a role in this particular neurological disorder (Ffytche et al., 2010; see also Kleinschmidt and Vuilleumier, 2013). Indeed, successful navigation in familiar environments not only involves the PHC, but also a wide range of occipital, medial parietal, temporal and frontal areas (meta-analysis in Boccia et al., 2014). Thus, a disconnection between the right PHC and other areas of this network may also play a role in this disorder.

Our goal was to investigate place recognition mechanisms in a stroke patient with damage including mainly the right PHC/hippocampus and part of the medial fusiform cortex. The location and extent of the lesion caused a severe prosopagnosia and a partial landmark agnosia (see Hecaen et al., 1980; McCarthy et al., 1996; Pallis, 1955; for similar cases of combined prosopagnosia and topographic agnosia following analogous lesions), providing the unique opportunity to disentangle successful versus unsuccessful place recognition mechanisms in the same participant. Photographs of personally familiar and unfamiliar places were displayed during event-related fMRI of an incidental categorization task (van Assche et al., 2016). An additional post-scan visual recognition test allowed classifying recognized versus unrecognized familiar places. We first examined the functional integrity of the right and left PHC during basic visualization of places, checking that the left but not right PHC region remained functionally active after the lesion. Then, we assessed the involvement of the PHC during the analysis of recognized (familiar) scenes as compared with unrecognized (familiar or unfamiliar) scenes by means of direct comparison, to specifically probe for brain processes associated with overt place recognition. Moreover, task-based functional connectivity was performed to illuminate the role of functional interactions during overt place recognition. If the PHC plays a fundamental role in this process, then it should be more recruited for recognized places in the patient, either in the contralesional and/or ipsilesional side. If not, the patient should show compensatory activity elsewhere during the recognition process.

2. Material and methods

2.1. Case report

Patient PR is a right-handed male, 68 years of age at the time of the present evaluation. He graduated from a university-level business school and is a businessman in the finance domain. One year prior to the current study, he had been admitted to the Neurology Unit of the Geneva University Hospital following a first minor cardio-embolic ischemic stroke involving the right parietal cortex and the occipital cortex bilaterally. The neurological status did not reveal any particular visual field defect. On this occasion, he underwent a series of standard neuropsychological tests assessing language, praxis, executive, memory, attention and visual-perceptual abilities (see *Supplementary Table 1*). This first neuropsychological testing revealed signs of associative visual agnosia, difficulties in verbal and visual episodic memory, and a mild executive impairment. All other assessed cognitive functions were unimpaired. In a second evaluation one month later (*Supplementary Table 1*), only verbal working memory difficulties and a mild executive impairment (inhibition) were observed. Signs of associative visual agnosia and verbal episodic memory difficulties had disappeared. Concerning visual episodic memory, his performance improved and was within the normal range, however from a clinical standpoint, immediate recall was estimated to be insufficient given his high educational level. At this time, PR continued working full-time as a business expert.

Ten months later, the patient was admitted again in the same unit due to unprecedented and acute visual complaints consisting in an inability to recognize close family members as well as slight difficulties in orientating himself in his neighborhood. The neurological status was normal, except a left superior quadranopsia which did not affect the following testing. During a third neuropsychological examination (*Supplementary Table 1*), PR was alert and fully cooperative. His expression was fluent, and his verbal comprehension intact. No visuo-constructive apraxia, neglect, or any other generalized visuo-spatial impairment was observed. Verbal episodic memory was intact. With reference to executive and attentional functions, PR showed mild difficulties in cognitive flexibility and selective attention (Bells' test). With regard to visuo-perceptive abilities, signs of associative agnosia were observed (Visual Object and Space Perception Battery; Birmingham Object Recognition Battery). For the evaluation of prosopagnosia, we used a standard battery from the Geneva University Hospital in addition to standard neuropsychological testing (Benton Face Recognition Test). The patient performed significantly worse than a control group (t-test Crawford & Garthwaite, 2007) at the recognition of famous faces (patient = 54% correct; control group = 77 ± 12% correct; $p < 0.01$), famous faces occupation sorting (matching semantic and visual inputs; patient: 56% correct; control group: 90 ± 9% correct; $p < 0.01$), gender identification (patient = 66%; control group = 92 ± 5% correct; $p < 0.01$), and at a short version of the Jane task (patient: 50% correct; control group = 80 ± 15% correct; $p < 0.01$; Mondloch et al., 2002; *Supplementary Table 2*).

Concerning the topographical domain (Table 1), the patient presented some difficulties in the identification of famous buildings (hesitation, latency, utilization of verbal strategies to facilitate the identification), and a significantly impaired ability to recognize places that are highly familiar for him (26/40 recognized familiar places; see post-scan procedure and results section). In contrast, tests assessing spatial representations were intact as judged by his normal performance on tests evaluating specific spatial abilities (i.e. landscape perspective test, cognitive map recall test, map drawing). Moreover, his capacity to navigate in the hospital was adequate (using both verbal and spatial strategies). In sum, PR presented a mild landmark agnosia, a severe prosopagnosia, signs of associative agnosia and very mild executive and attentional difficulties.

Table 1
Neuropsychological assessment of the patient's topographical abilities (impaired performance in bold).

Landmark identification	
Identification of famous buildings	**19/23, hesitations, latencies**
Egocentric space	
Landscape Perspective Test[1]	
Rotational movement	6/7
Translational movement	4/6
Road-Map Money test[2]	32/32
Allocentric space	
Localization of landmarks on a map	Ok
Spatial cognition about familiar environments	
Identification of personally familiar places (see results section)	**26/40**
Familiar egocentric space: Route description	Ok
Familiar allocentric space:	
Cognitive Map Recall test[1]	17/24
Map and route drawing	Ok
Spatial cognition about unfamiliar environments	
Navigational abilities in the hospital	Ok

[1] Descloux et al. (2015).
[2] Money et al. (1965).