

## RAPID COMMUNICATION

## Visual Recognition Memory: A Double Anatomo-Functional Dissociation

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**ABSTRACT:** There is an ongoing debate regarding the respective role of anterior subhippocampal structures and the hippocampus in recognition memory. Here, we report a double anatomo-functional dissociation observed in two brain-damaged patients, FRG and JMG. They both suffered from complete destruction of left MTL structures. In the right hemisphere however, FRG sustained extensive lesions to the hippocampus sparing anterior subhippocampal structures, while JMG suffered from the reversed pattern of lesion, i.e., extensive damage to anterior subhippocampal structures but preserved hippocampus. FRG was severely amnesic and failed all recall tasks involving visual material, but exhibited normal performance at a large battery of visual recognition memory tasks. JMG was not amnesic and showed the opposite pattern of performance. These results strongly support the view that right anterior subhippocampal structures are a critical relay for visual recognition memory in the human. © 2010 Wiley-Liss, Inc.

**KEY WORDS:** recognition memory; human; neuropsychology

Recognition memory refers to the ability to judge whether a stimulus has previously been encountered. There are large disagreements over how this is performed (Murray et al., 2007; Squire et al., 2007). In particular, the brain areas subserving this ability and the way they interact with each other are among the key questions remaining in dispute.

Patients with developmental amnesia and lesions restricted to the hippocampus have been shown to perform normally on tasks of recognition memory (Vargha-Khadem et al., 1997). These results have suggested that preservation of the visual ventral pathway, up to the highest areas in this hierarchy such as the perirhinal cortex, allows normal recognition under some circumstances (Murray et al., 2007). Convergent results observed in patients who sustained isolated lesions to the hippocampus at an adult age further strengthened this idea (Mayes et al., 2002; Bastin et al., 2004; Aggleton et al., 2005; Barbeau et al., 2005). However, a

definite conclusion has not been drawn since impaired recognition memory in patients with similar lesions have simultaneously been reported (Manns et al., 2003; Kopelman et al., 2007). Thus, the conditions under which recognition memory may be preserved after isolated lesions to the hippocampus remain elusive (Holdstock et al., 2008) and more studies are clearly necessary. Here, we report a double anatomical dissociation aimed at bringing further insights into this issue.

Patient FRG, a female patient, was already reported in detail by Barbeau et al. (2005). She suffered from herpes simplex encephalitis that left her densely amnesic when she was 44-year-old. Neuropsychological evaluation was performed at the age of 48. Her delayed WMS-R MQ was 57 (mean = 100, standard deviation (SD) = 15, Wechsler, 1991). Like most severely amnesic patients, she had lost her autonomy because she quickly forgot any event and was lost in time and space. Despite considerable difficulties with all tasks requiring recall of verbal and visual material, along with tasks assessing verbal recognition memory, her performance at visual recognition memory tasks was overall preserved. She obtained normal scores at 14 out of 18 different tasks based on a wide variety of stimuli and procedures. Her overall Z-score on visual recognition memory tasks was  $-0.77$ .

FRG sustained complete destruction of the left medial temporal lobes. In the right hemisphere however, the hippocampus was extensively damaged while anterior subhippocampal structures (medial temporal pole, perirhinal, and entorhinal cortices) were largely preserved (Figs. 1 and 2). As supported by the literature, her amnesic syndrome was related to the bilateral destruction of the hippocampus, while her preserved performance on visual recognition memory tasks was related to the preservation of her right anterior subhippocampal structures.

In this study, we report a new patient, JMG, with similar MTL left-sided lesions, and the exact opposite pattern of lesion on the right side. This male patient suffered from a meningo-encephalitis, presumably from a herpes origin, at the age of 20. He was 54 at the

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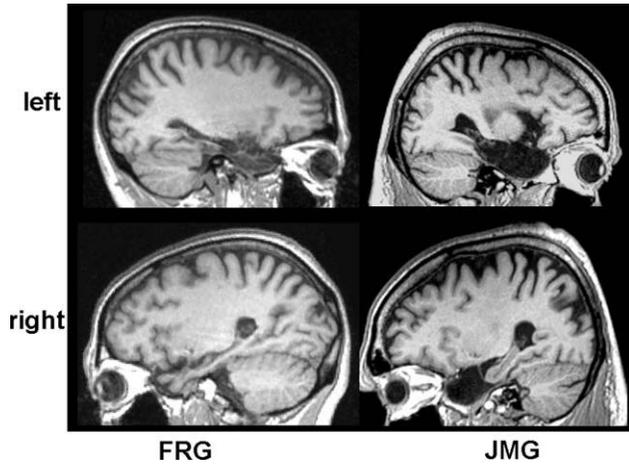
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**FIGURE 1.** FRG and JMG lesions. Upper row: sagittal slices of the left hemisphere showing massive destruction of all MTL structures in both patients. Lower row: sagittal slices of the right hemisphere showing an opposite pattern of lesions. In FRG, right subhippocampal structures are largely preserved while the hippocampus is severely lesioned (some residual tissue can be observed within the right hippocampal area, but displaying large signal abnormalities on FLAIR sequences). In JMG, the right hippocampus was preserved while subhippocampal structures were severely lesioned, as indicated by the position of the hippocampus which plunges toward the temporal floor instead of remaining parallel to it.

time of this study. He was not amnesic according to usual standards, although his memory efficiency was low. His delayed WMS-III MQ was 71 (Wechsler, 2001). He was however able to conduct his life normally, got married, and has been working by himself as a hairdresser, managing his own barbershop. He was not lost in time (for example, he could easily handle his appointments with his customers and make plans for his life and business) nor in space (for example, he enjoyed biking alone and completed an average of 14,000 km every year).

His MRI revealed complete left MTL destruction very similar to that of FRG. On the right side however, only the hippocampus was preserved. Right subhippocampal structures (temporal pole, entorhinal, perirhinal) were either completely destroyed or severely damaged, with the exception of the parahippocampal cortex that was damaged laterally but not medially. Figure 1 provides a general view of the anatomical dissociation between FRG and JMG in the sagittal plane. Figure 2 provides a detailed comparison of both patients in the coronal plane. JMG's right hippocampus was thought to be largely functional because: (1) there was no evidence of abnormal signal on anatomical MRI slices; (2) JMG was not amnesic and remained fully able to carry out his life despite large MTL lesions; (3) JMG routinely performed activities requiring a high level of spatial cognition, including biking in unfamiliar environments, a feat difficult to conciliate with the absence of functional hippocampal tissue. In summary, both patients displayed a complete destruction of the entire left MTL structures. On the right side, however, FRG exhibited relative preservation of subhippocampal structures and destruction of the hippocam-

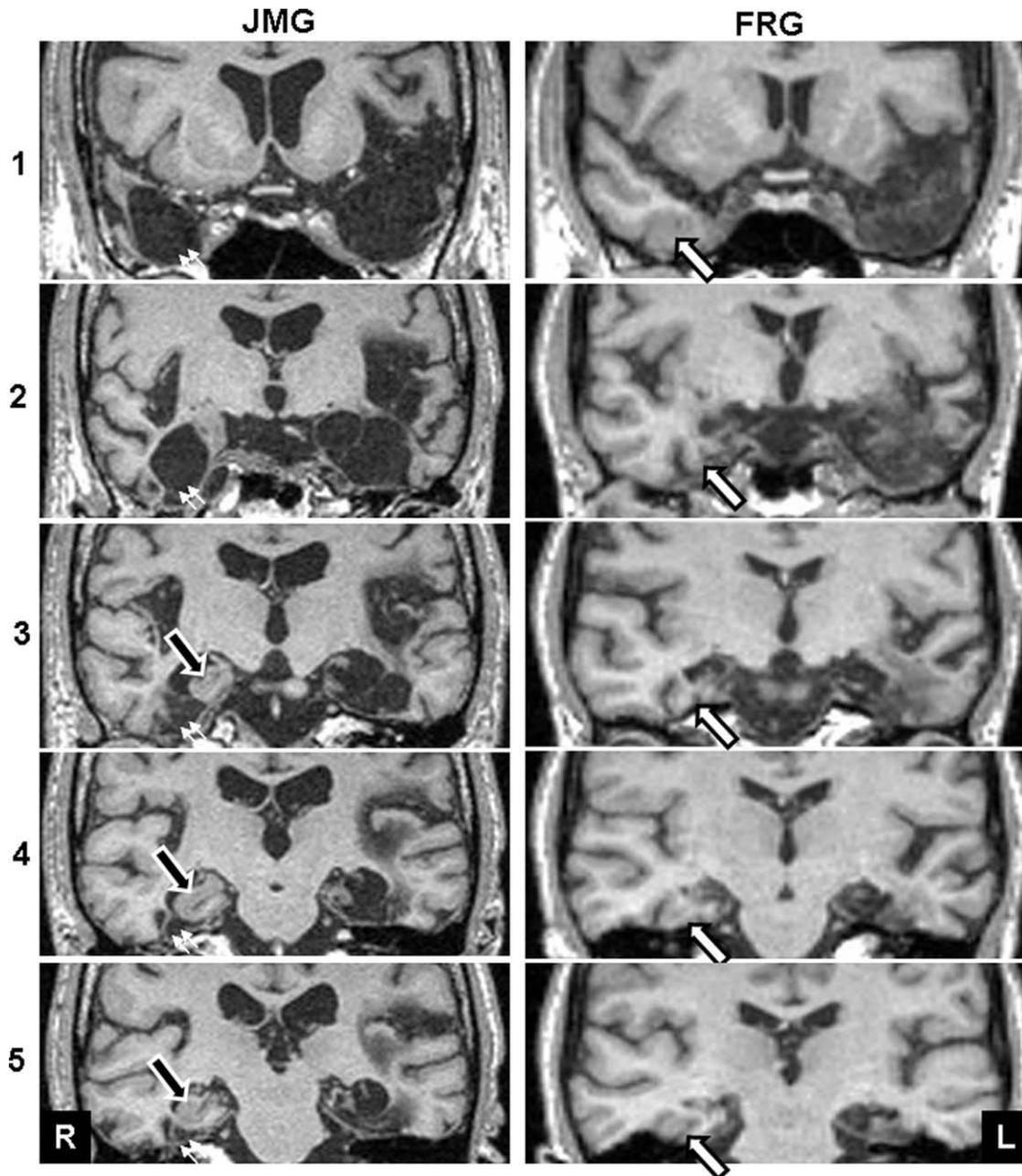
pus, while JMG showed a preservation of the hippocampus and a severe destruction of subhippocampal structures. In the face of this double anatomical dissociation, we evaluated the possibility of a double functional dissociation.

JMG was in a similar age range than FRG when the present assessment was undertaken (54 against 48 for FRG). They had similar global cognitive functioning as measured by global IQ (JMG: 90; FRG: 94, WAIS-III, Wechsler, 2000), and they suffered from the same disease (herpes simplex encephalitis confirmed in FRG, presumed in JMG). Comparison of behavioral performance obtained by the two subjects was thus methodologically suitable. JMG underwent exactly the same set of recall and recognition memory tasks that FRG had undergone (Barbeau et al., 2005). Since they were in a similar age range, the same normative data set employed with FRG was used. Therefore, all tasks and norms used in JMG's evaluation were fully independent from the present study. We also used the same cut-off of impairment, that is, a performance below 2SD of the mean values obtained by control subjects.

We first compared JMG's and FRG's performance in the verbal modality. Both recall and recognition tasks were impaired to a similar extent (recall tasks,  $n = 4$ , FRG mean  $Z$ -score =  $-3.72$ ,  $SD = 1.06$ , JMG =  $-3.05$ ,  $SD = 1.34$ ; recognition tasks,  $n = 6$ , FRG =  $-4.77$ ,  $SD = 3.11$ , JMG =  $-5.11$ ,  $SD = 3.34$ ).

We then compared performance in the visual modality. Whereas JMG performed within normal limits across all tasks of visual recall ( $n = 4$ ), FRG performed systematically well below cut-off (Table 1). The inverse pattern was however observed for visual recognition memory tasks. While FRG's mean  $Z$ -score was within normal limits ( $n = 18$  tasks,  $-0.77$ ,  $SD = 2.06$ ), JMG's average performance was severely impaired ( $-4.78$ ,  $SD = 5.69$ ). The difference between the performance obtained by the two patients was significant either comparing means (two-tailed  $T$ -test with equal variance not assumed,  $t(21.38) = 2.81$ ,  $P = 0.01$ ) or using a statistical procedure insensitive to outliers (two-tailed Mann-Whitney U test,  $U = 66$ ,  $P = 0.002$ ). We used two-tailed nonparametric Mann-Whitney U tests to compare performance on tests of visual recall and visual recognition. Contrary to FRG, whose visual recall scores were more impaired than visual recognition scores ( $n = 4$  vs.  $n = 18$ ,  $U = 10$ ,  $P = 0.03$ ), JMG's recall of visual material was significantly better than visual recognition ( $U = 4$ ,  $P = 0.006$ ). Of note however, such statistical comparisons are valid under the assumption that recall and recognition sets of observations are independent. This assumption is violated within-sample, which may temper the validity of our comparisons, since recall, or recognition tests, assess a similar ability. These results argue for a double functional dissociation pattern between these two patients (Fig. 3).

Compared with FRG, JMG systematically performed lower on visual recognition memory tasks with the exception of two tasks requiring recognition of animals and scenes (Tasks 10 and 12, Table 2). Both FRG and JMG were similarly impaired relative to controls when recognizing animals but normal when recognizing scenes.



**FIGURE 2.** Coronal slices from anterior (top) to posterior (bottom) MTL structures. Note the massive destructions of all MTL structures in the left hemisphere of both patients as well as lesions extending to the insula bilaterally in JMG. In the right hemisphere, the white arrows with black outline indicates the remaining subhippocampal structures in FRG. They are

largely preserved from anterior to posterior regions while corresponding regions have been damaged in JMG (small double arrows). Conversely, the black arrows with white outline indicates the spared hippocampus in JMG, which is absent in FRG (some residual tissue can be observed but see legend of Figure 1). R, right; L, left.

Overall, FRG was impaired at four tests of visual recognition memory. However, her performance remained well above chance, her impairment being related to small standard deviations within the control subjects population as previously discussed (Barbeau et al., 2005). Compared with control subjects, JMG performed well below the established cut-off (2SD) at 10 out of 18 visual recognition tasks (Table 2). Performance at 8 tasks were thus above the usual cut-off for impaired perform-

ance. With the exception of the already mentioned recognition of scenes, performance on these tasks was however within the low normal range ( $n = 7$ , mean =  $-1.64$ , SD =  $0.25$ ). Furthermore, performance at four of these seven tasks was close to chance, performance above  $-2SD$  being related either to a lack of sensitivity of scaled scores for such low performance (Tasks 2, 3, 4), or to task difficulty for control subjects (but notably less difficult for FRG,  $Z$ -score =  $+2.33$ , Task 18). What

TABLE 1. *Performance of FRG and JMG on Visual Recall Tasks*

Tests of visual recall	FRG Z-score	JMG Z-score
1 Rey Osterreich complex figure (Rey, 1959)	-3.07	-0.25
2 Figure reproduction II subtest (WMS-R) (Wechsler, 1991)	-3.30	1.03
3 Shapes subtest (Doors and People test) (Baddeley et al., 1994)	-2.88	-0.67
4 Family scenes II subtest (WMS-III) (Wechsler, 2001)	-3.00	-1.33
Mean	-3.06	-0.31
SD	0.18	1.00

remains however is that JMG's performance was sometimes well above chance, contrary to what would have been expected in the complete absence of recognition ability (notably Task 9, chance = 25%; JMG = 65%,  $Z$ -score = -1.15; task 10, chance = 50%, JMG = 80%,  $Z$ -score = -2.20).

The contrast between both patients is striking, one being amnesic but succeeding on visual recognition memory tasks, the other being not amnesic and succeeding relatively well on tasks of visual recall but showing overall severe impairment of visual recognition memory. JMG's low performance cannot be ascribed to visual difficulties since he performed within normal limits at all visual recall tasks and at several standardized visual perceptual batteries (VOSP, Warrington and James, 1985; BORB, Riddoch and Humphreys, 1993). It is interesting to note that 13 out of the 18 visual recognition memory tasks took place immediately or not more than 3 min after the encoding phase, which may have prevented JMG's overall performance of being even lower. In contrast, FRG's performance remained normal after a one-week delay. Another crucial point is that JMG was most impaired at the three tasks that used incidental encoding (DMS48, Tasks 6, 7, 8; Barbeau et al., 2004). In this case, JMG was not warned that he would be assessed on his ability to later recognize the stimuli. His low performance appears difficult to relate to attentional fluctuations since he was very dedicated and involved during the whole testing procedure, and his working memory index reached the 87th percentile at the WMS-III. Performance at the DMS48 is hypothesized to strongly rely on the same natural system that allows the encoding of many items from our environment without making any effort and being aware of it. Thus, this process may strongly depend on the integrity of the visual ventral stream, as suggested by FRG's preserved performance on these tasks.

In summary, we report in this study a double anatomo-functional dissociation between two patients demonstrating that visual recognition memory critically relies on right subhippocampal structures. This double-dissociation greatly strengthens and extends the findings of previous studies which have reported single-dissociations in patients with isolated lesions to the hippocampus (Mayes et al., 2002; Bastin et al., 2004; Aggleton et al., 2005; Barbeau et al., 2005).

In addition, the right hippocampus does not seem in itself able to support visual recognition memory. Indeed, we could show that JMG had a right hippocampus that was preserved both anatomically and functionally (most notably, recall of visual material was within normal limits, as reported in this study). If the right hippocampus plays a role in visual recognition memory, this process therefore stands after a first stage mediated by anterior subhippocampal structures. This result is in line with studies in nonhuman primates (Meunier et al., 1993; Buffalo et al., 1999) and argues against a view that anterior subhippocampal structures and the hippocampus are functionally homogeneous.

Bowles et al. have reported the case of NB, a patient with isolated lesions to the left perirhinal cortex that spared the hippocampus following surgery for intractable epilepsy (Bowles et al., 2007). NB's evaluation demonstrated impaired familiarity but preserved recollection, supporting the idea that these memory processes rely on different MTL structures and that lesions of anterior subhippocampal structures impair specific memory processes. Although these results are convergent with our present findings with JMG, they may also plead against our contention that recognition memory involves a mandatory subhippocampal stage, as NB's performance on recognition memory tasks was overall preserved. However, NB's performance proved to be in fact impaired when assessed using short delays in a response deadline procedure. Furthermore, there are notable differences between the two studies. First, words were used in NB's study. However, it has been suggested that the hippocampus could play a material-specific role in recognition memory, particularly regarding words (Bird and Burgess, 2008). Second, NB's lesion was unilateral (sparing right-sided MTL structures) and of much smaller volume than that of JMG, suggesting alternative pathways could be used.

Overall, our interpretation is that anterior subhippocampal structures perform critical computations, presumably perceptivo-mnesic (Barbeau et al., 2008; Maillard et al., in press), that dis-

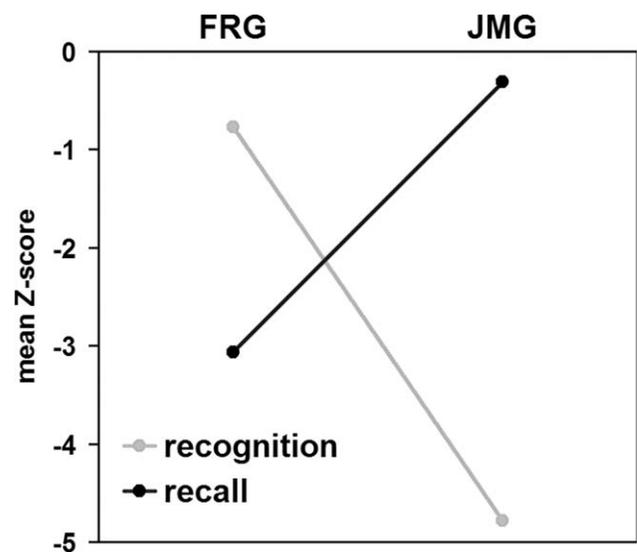


FIGURE 3. Comparison of the performance of FRG, JMG on the visual recall and recognition memory tasks showing a double dissociation.

TABLE 2.

Performance of FRG and JMG on 18 Visual Recognition Memory Tasks

	Test description	Stimulus type	Paradigm	Chance level	FRG perf. %	JMG perf. %	FRG Zscore	JMG Zscore
1	Doors and Peoples Test—Part A (Baddeley et al., 1994)	Doors	FC	0.25	0.92	0.58	0.00	-1.96
2	Doors and Peoples Test—Part B (Baddeley et al., 1994)	Doors	FC	0.25	0.42	0.33	-1.28	-1.64
3	WMS-III face recognition subtest immediate (Wechsler, 2001)	Faces	Y/N	0.50	0.60	0.54	-1.33	-1.67
4	Same test as 3, delayed	Faces	Y/N	0.50	0.73	0.56	0.00	-1.67
5	RMT face recognition test (Warrington, 1984)	Faces	FC	0.50	0.71	0.62	-2.85	-3.75
6	Delayed-Matching to Sample with trial-unique distractors task, 3 mn (Barbeau et al., 2004)	Various objects	FC	0.50	0.92	0.71	-3.50	-14.08
7	Same test as 6, delayed 60 mn	Various objects	FC	0.50	0.98	0.65	-0.50	-17.21
8	Same test as 6, delayed one week	Various objects	FC	0.50	0.96	0.58	-0.33	-12.89
9	Forced-choice test with 3 distractors per targets	Various objects	FC	0.25	0.88	0.65	0.62	-1.15
10	Yes/No recognition test with 25 targets and 25 distractors	Animals	Y/N	0.50	0.76	0.80	-3.03	-2.20
11	Yes/No recognition test with 25 targets and 25 distractors	Buildings	Y/N	0.50	0.72	0.68	-1.20	-2.00
12	Yes/No recognition test with 25 targets and 25 distractors	Scenes	Y/N	0.50	0.84	0.86	0.23	0.50
13	Yes/No recognition test with 25 targets and 25 distractors	Fruits and Vegetables	Y/N	0.50	0.78	0.62	-6.12	-15.50
14	Yes/No recognition test with 25 targets and 25 distractors	Tools	Y/N	0.50	0.92	0.76	0.65	-2.60
15	Yes/No recognition test with 15 targets and 30 distractors. Free learning and recognition delay	Abstract pattern	Y/N	0.33	0.87	0.73	0.17	-1.82
16	Yes/No recognition test with 15 targets and 30 distractors. 800 ms learning and recognition delay	Abstract pattern	Y/N	0.33	0.91	0.62	2.08	-2.81
17	Yes/No recognition test with 15 targets and 30 distractors. 400 ms learning and recognition delay	Abstract pattern	Y/N	0.33	0.76	0.60	0.14	-2.03
18	Forced-choice test with long delay between study and test	Abstract pattern	Y/N	0.50	0.78	0.58	2.33	-1.6
						Mean	-0.77	-4.78
						SD	2.06	5.69

% performance is the overall accuracy (correct recognition of targets and rejection of distractors). FC: forced-choice, Y/N: yes/no recognition memory task. Supplementary details about the tasks can be found in Barbeau et al. (2005).

rupt recognition memory. This interpretation is in line with models holding that information critical for single-item processing reach the hippocampus after a first stage of processing within anterior subhippocampal structures (Mishkin et al., 1997; Lavenex and Amaral, 2000). A possibility is that our results mainly stand for visual material and right MTL structures. During visual recognition memory tasks, stimuli need to be individualized at the exemplar level. This individualization strongly relies on the fine grained visuo-perceptive analysis of intrinsic stimuli characteristics before allowing the appropriate matching with memory traces. It may be these operations that are impaired after right subhippocampal structures lesion. The present study

does not speak directly to the debate about single- vs. dual-process models of recognition memory (Squire et al., 2007). For example, we did not assess familiarity or recollection formerly. However, our results suggest that perceptivo-mnesic processes, and how they relate to familiarity and recollection, should also be components of any model of recognition memory.

This interpretation of our results could further explain why JMG was not helped by recall when required to recognize stimuli. This very unusual pattern can be explained by the difference in the stimuli used in recognition and recall tasks. In recognition memory tasks, stimuli are usually pictures of objects requiring some kind of individualization, which may require a subhippo-

campal stage as suggested above. In recall tasks on the other hand, line-drawings of geometrical shapes are usually used. These stimuli may rely less on visuo-perceptive but more on visuo-spatial characteristics and may thus be processed through other circuits than anterior subhippocampal structures.

JMG's recognition memory scores were not always at the chance level. He notably performed normally at a scene recognition task. To account for this finding, it is reasonable to hypothesize that the remaining JMG's right parahippocampal cortex endorses the processing of this kind of stimuli, given the well-known implication of this structure in scene processing (Epstein, 2008). Taken together, although the main ventral visual pathway supporting recognition memory is damaged in JMG, alternative pathways may help him process adequately certain classes of stimuli, leading to variable performance across visual recognition memory tasks during formal testing.

To conclude, patient FRG, in contrast to JMG, performed within the normal range at a large variety of recognition memory tasks, even when facing briefly presented stimuli (400 ms), during both encoding and recognition phases. She also performed well when incidental encoding was used, in contrast to JMG. The right ventral pathway may thus play a crucial role for automatic encoding, fast recognition and perceptivo-mnesic processes (Mandler, 1980; Brown and Aggleton, 2001). Furthermore, it acts as a cognitive system on its own, as results obtained with FRG and JMG indicate that the right hippocampus is not necessary, or even able to support normal visual recognition memory.

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