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Selective lesion to the entorhinal cortex leads to an impairment in familiarity but not recollection

Karen R. Brandt [a,*], Michael W. Eysenck [a], Maria Kragh Nielsen [a], Tim J. von Oertzen [b,c]

[a] University of Roehampton, London, United Kingdom
[b] Atkinson Morley Neuroscience Centre, St. George's Hospital, London, United Kingdom
[c] Department of Neurology 1, Neuromed Campus, Kepler Universitaetsklinikum, Linz, Austria

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ABSTRACT

The present research explored the effects of selective impairment to the entorhinal cortex on the processes of familiarity and recollection. To achieve this objective, the performance of patient MR, who has a selective impairment of the left entorhinal cortex, was compared to that of age and IQ-matched controls. Four experiments tested participants' recognition memory for familiar and unfamiliar faces and words. In all experiments, participants studied lists of items and then completed an old/new recognition test in which they also made remember/know/guess judgements. A fifth experiment tested participants' priming associated with the familiarity process. MR had intact performance in both face recognition experiments as well as having intact performance in pseudoword recognition. Crucially, however, in the familiar word experiment, whilst MR performed similarly to control participants in terms of recollection, she showed a marked impairment in familiarity. Furthermore, she also demonstrated a reversed conceptual priming effect. MR's impairment is both material-specific and selective for previously encountered but not new verbal items (pseudowords). These findings provide the first clear evidence that selective impairment of the entorhinal cortex impairs the familiarity process for familiar verbal material whilst leaving recollection intact. These results suggest the entorhinal cortex does not have attributes reflective of both recollection and familiarity as previously assumed, but rather supports context-free long-term familiarity-based recognition memory.

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1. Introduction

One of the main ways episodic memory has been assessed is through various tests of recognition memory. At the theoretical level, there has been much controversy as to whether performance on recognition memory tests reflects one or two underlying processes. According to advocates of single-process theories (e.g., Dunn, 2008), what is important is the strength of the underlying memory trace. Recollection judgments (based on retrieval of contextual information) are simply based on stronger memory traces than familiarity judgments (based solely on subjective familiarity). Thus, the differences among memory traces are quantitative rather than qualitative. Dunn (2008) claimed support for this theoretical assumption in his meta-analysis of 37 studies using the remember-know task. However, according to advocates of dual-process theories (e.g., Gardiner & Java, 1993; Yonelinas, 2001, 2002), there are separate processes of familiarity and recollection. Familiarity is the process of recognising an item because of its perceived memory strength in the absence of conscious retrieval of contextual information. Hence familiarity can be seen as being on a continuum with a cut-off point that distinguishes new from old items. It is a process of intra-item sensory and perceptual integrations and these integrations are a set of continuous processes. So frequent occurrences increment the integration of an event and result in higher confidence familiarity judgements whereas items that are weakly integrated give rise only to a general feeling of familiarity. In contrast, recollection is the process of recognizing an item on the basis of conscious retrieval of relevant contextual information.

A current issue in cognitive neuroscience research is whether or not the distinction between recollection and familiarity is rooted in differential contributions to recognition made by different areas within the medial temporal lobe (Montaldi & Mayes, 2010). According to Aggleton and Brown (1999), there are two distinct memory systems originating within the medial temporal lobes:

* Corresponding author at: Department of Psychology, Whitelands College, University of Roehampton, Holybourne Avenue, London SW15 4JD, United Kingdom.
E-mail address: karen.brandt@roehampton.ac.uk (K.R. Brandt).

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the extended hippocampal system comprising the hippocampus, the anterior nucleus of the thalamus, the mamillothalamic tract, and the perirhinal system comprising the perirhinal cortex and the mediodorsal nucleus. Whereas the hippocampal system subserves the process of recollection, the perirhinal system subserves the process of familiarity. Substantial evidence supports this view demonstrating that hippocampal damage results in selective impairment of recollection but not familiarity (Brandt, Gardiner, Vargha-Khadem, Baddeley, & Mishkin, 2009; Holdstock et al., 2002; Mayes et al., 2004; Yonelinas, 2002). However, there is also some research showing impairments of both recollection and familiarity in hippocampal patients (Knowlton & Squire, 1995; Manns, Hopkins, Reed, Kitchener, & Squire, 2003).

In addition, Aggleton and Brown's model (1999) is supported by fMRI research on healthy participants. Diana, Yonelinas, and Ranganath (2007) found in a meta-analysis that recollection was associated with more activation in the hippocampus than the perirhinal cortex, whereas familiarity was associated with more activation in the perirhinal cortex than the hippocampus. de Vanssay-Maigne et al. (2011) supported and extended the findings of Diana et al. (2007). Of most relevance here, old words correctly recognized with a sense of familiarity differed from those not recognized (i.e., familiarity effect), in that the former were associated with greater bilateral activation in the entorhinal cortex and perirhinal cortex at retrieval. Whilst the familiarity effect was not related to any hippocampal activations, thereby supporting Aggleton and Brown's model, the recollection effect was related to both hippocampal and non-hippocampal activations (e.g., perirhinal cortex, entorhinal cortex), providing less support for the model.

Whilst there has been substantial support for the role of the hippocampus in recollection, in order to provide stronger support for dual-process theories, support must also be shown for the role of the perirhinal system in the process of familiarity. Some have argued that the processes supporting familiarity (explicit recognition) are similar to those supporting implicit conceptual priming and demonstrate a strong relationship between the perirhinal cortex and these two types of recognition (Rajaram & Geraci, 2000; Wang, Lazzara, Ranganath, Knight, & Yonelinas, 2010; Wang & Yonelinas, 2012). For example, Wang et al. (2010) found that increased perirhinal cortex activity was associated with conceptual priming and that medial temporal lobe patients with perirhinal cortex damage (but not hippocampal damage) were impaired both on conceptual priming and familiarity. Furthermore, in a later study, Wang and Yonelinas (2012) tested the prediction that familiarity, but not recollection, relied on the same processes that support conceptual implicit memory. Their results demonstrated that whereas recollection did not correlate with any of their three conceptual priming effects, the process of familiarity did. However, there has also been evidence to suggest that familiarity and conceptual priming rely on distinct neural processes. Voss, Reber, Mesulam, Parrish, and Paller (2008) found that whereas conceptual priming was associated with decreased left prefrontal cortex activity, familiarity was associated with increased right parietal cortex activity. Thus, at present, the relationship between familiarity and conceptual priming and how the perirhinal system supports these processes, remains unresolved.

One way to resolve this issue and to provide stronger support for dual-process theories would be to demonstrate a double dissociation in which some patients performed at a comparable level to healthy controls on familiarity and conceptual priming, but were severely impaired on recollection whereas others patients showed the opposite pattern. The pattern of relatively greater impairment of recollection than of familiarity in patients with hippocampal damage is consistent with several dual-process theories. However, it can be argued that it is also consistent with single-process theories. On the assumption that patients with hippocampal damage have weaker memory traces than healthy controls, it follows that their recognition memory performance should be especially poor when successful performance requires strong memory traces (recollection) than when weaker memory traces will suffice (familiarity).

The discovery of patients showing greater impairment of familiarity than of recollection would therefore provide especially strong support for dual-process accounts and would also be hard to interpret within single-process theories. Precisely this pattern has been reported in studies by Bowles and colleagues on a female patient (NB) who had a left unilateral lesionectomy for intractable epilepsy (Bowles et al., 2007; Martin, Bowles, Mirsattari, & Köhler, 2011). This surgery removed 83% of her amygdala, 43% of her perirhinal cortex and 59% of her entorhinal cortex.

Bowles et al. (2007) carried out several experiments in which they assessed NB's familiarity and recollection for words in various paradigms. The consistent finding was that NB had impaired familiarity combined with intact recollection. Martin et al. (2011) pointed out that there is evidence that left-hemisphere areas are of particular importance in the learning and remembering of verbal materials whereas right-hemisphere areas are relatively more important with non-verbal stimuli (Lee, Yip, & Jones-Gotman, 2002). Accordingly, they assessed NB's familiarity and recollection judgments for non-words, abstract pictures and faces. NB's recollection performance was comparable to that of healthy controls for all three types of material. In contrast, her familiarity performance was significantly below control performance with non-words but was intact with abstract pictures and faces.

The totality of the findings from these two studies indicates that NB has consistently impaired familiarity performance with verbal materials (words or non-words). In contrast, she has intact familiarity performance with non-verbal materials. This lateralisation effect is firstly consistent with the contention that the left hemisphere supports the learning and retention of verbal material (Martin, 1999; Milner, 1972) whereas the right hemisphere supports memory for nonverbal material (Kimura, 1963; Martin, 1999). Secondly, it supports research showing a marked impairment in verbal memory in left compared to patients with right unilateral temporal lobe epilepsy (Hendriks et al., 2004; Kim, Yi, Ik Son, & Kim, 2003) as well as for unfamiliar verbal memory (Falk, Cole, & Glosser, 2002) and in the process of familiarity (Aly, Knight, & Yonelinas, 2010). More importantly, the findings are consistent with the predictions of dual-process theories when combined with the additional hypothesis that the left perirhinal system is primarily involved in familiarity processing of verbal stimuli (de Vanssay-Maigne et al., 2011).

The findings of Bowles et al. (2007) and Martin et al. (2011) are of considerable theoretical importance. These findings (taken in conjunction with those on patients with selective hippocampal damage) support the double dissociation between familiarity and recollection within the medial temporal lobes predicted by dual-process theories. However, there are various reasons why it is necessary to extend this research. First, NB has damage including the amygdala, perirhinal cortex and entorhinal cortex. Thus, it is not possible to pinpoint the brain areas most crucial for familiarity judgments. Second, whilst their research employed unfamiliar verbal (non-words) and non-verbal (abstract pictures, faces) material, only the addition of verbal material that was familiar was used. Hence the non-verbal material was entirely unfamiliar to NB and the controls, whereas all the verbal material (with the sole exception of non-words) was familiar to them. The use of non-verbal familiar material (e.g., faces of celebrities) would clarify whether the left perirhinal system is involved in the familiarity process for familiar non-verbal stimuli. Third, NB's conceptual priming was not measured and therefore cannot shed light on how such a

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