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Research report

Damage to the lateral prefrontal cortex impairs familiarity but not recollection

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ABSTRACT

Frontal lobe lesions impair recognition memory but it is unclear whether the deficits arise from impaired recollection, impaired familiarity, or both. In the current study, recognition memory for verbal materials was examined in patients with damage to the left or right lateral prefrontal cortex. Words were incidentally encoded under semantic or phonological orienting conditions, and recognition memory was tested using a 6-point confidence procedure. Receiver operating characteristics (ROCs) were examined in order to measure the contributions of recollection and familiarity to recognition memory. In both encoding conditions, lateral prefrontal cortex damage led to a deficit in familiarity but not recollection. Similar deficits were observed in left and right hemisphere patients. The results indicate that the lateral prefrontal cortex plays a critical role in the monitoring or decision processes required for accurate familiarity-based recognition responses.

Determining the neural substrates of episodic memory has been the focus of decades of research, beginning with the classic case of H.M., which revealed the importance of the medial temporal lobes [1]. In recent years, the contribution of the prefrontal cortex (PFC) to episodic memory has received growing attention. Frontal lobe lesions lead to a variety of subtle but noticeable memory impairments, particularly in the strategic control of encoding and retrieval [2–7]. Frontal patients perform poorly on many long-term memory tasks, including free recall, cued recall, and source and temporal order memory [see Refs. [2,8–10] for reviews]. They also show increased susceptibility to interference [e.g., Ref. [11]] and have difficulty with strategy implementation at encoding and retrieval, which extends to the organization and monitoring of retrieval from remote memory [12,13].

The body of research on long-term memory deficits in patients with frontal lesions has focused largely on memory tasks that involve some degree of strategy implementation at study, test, or both, and considerable progress has been made in understanding the strategic memory deficits in these patients. What has received less attention is a precise understanding of how the PFC contributes to item recognition, where the demand for strategic retrieval processes is minimized. Although item recognition was initially thought to be preserved in PFC patients [14], it is now apparent that PFC lesions do in fact impair recognition memory [see Ref. [10] for a meta-analysis]; nevertheless, the nature of this impairment is undetermined.

It is widely agreed that two retrieval processes support recognition memory judgments: recollection and familiarity [see Ref. [15] for a review]. Recollection reflects the retrieval of qualitative information about the study episode, such as where or when an event took place, or one's thoughts and feelings at the time. On the other hand, familiarity drives memory performance without any qualitative details coming to mind about where or when the item was encountered before. An extensive body of patient and neuroimaging research has focused on the role of the medial temporal lobes in recollection and familiarity [see Ref. [16] for review]. In the past 10 years, the role of the frontal lobes in recollection and familiarity has received growing attention in neuroimaging studies [Refs. [17–22]; see Ref. [23] for review], but there are only a handful of patient studies that address this issue. The consequence of frontal lobe lesions on recollection and familiarity, therefore, is not well established.

On theoretical grounds, there is good reason to think that the PFC may be important for both recollection and familiarity. Some indirect evidence comes from task comparisons, which show that source memory, which depends heavily on recollection, is impaired in PFC patients, while item memory, which can be supported largely by familiarity, is less impaired [e.g., Ref. [14]]. Moreover, recollection is often characterized as reflecting a controlled or strategic retrieval process, similar to that underlying free recall, whereas familiarity is thought to be a more automatic process. As such, one might predict that the frontal lobes are particularly critical for recollection [e.g., Refs. [24–28]]. On the other hand, familiarity is often characterized as a signal-detection retrieval process, which necessitates both an assessment of memory strength and a decision process, which involves setting response criteria for classifying

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items as old or new [e.g., Refs. [29,30]]. Both of those components of familiarity assessment may depend on the monitoring and evaluation processes supported by the PFC [see Ref. [18]].

We focus here on lateral prefrontal cortex (LPFC), which is richly connected with regions in the medial temporal lobe [see Ref. [31]] and has been directly implicated in item recognition in numerous previous studies [see Ref. [10] for review]. There are only a handful of studies investigating recollection and familiarity in LPFC patients, and these studies have yielded conflicting results. Most of the studies have utilized the remember/know procedure [32] to estimate the contributions of recollection and familiarity. This procedure requires participants to introspect on their memory experience and report whether they consciously 'remember' studying an item, or merely 'know' that an item was studied, without any qualitative details coming to mind about the study event. Most recently, Kishiyama et al. [33] found that recollection and familiarity were reduced in LPFC patients, following intentional encoding of pictures. In contrast, Duarte et al. [34] found that LPFC patients were impaired in familiarity, but not recollection, and the deficit was restricted to pictures presented to the lesioned hemisphere. Left LPFC patients were additionally impaired at remembering the context which items were encoded, suggesting that an objective measure of recollection was impaired in these patients, although self-reports of recollection were intact. Finally, an earlier study found that LPFC patients were not impaired at 'remembering' or 'knowing', although 'know' responses were slightly reduced [35]. Familiarity estimates, however, were not reported.

Another way of estimating the contributions of recollection and familiarity to recognition memory is to use receiver operating characteristics (ROCs), and fit the dual process signal detection model to the data [36,37]. This method allows one to estimate recollection and familiarity without relying on the subjective reports of the remember/know technique. The only ROC study with frontal lobe patients found that LPFC patients were impaired at familiarity, but not recollection, for incidentally encoded pictures [38].

Thus, there are some studies suggesting that recollection and familiarity are both intact in LPFC patients [35], other studies indicating that familiarity is impaired but recollection is not [34,38], and yet other studies suggesting that both recollection and familiarity are impaired [[33,34] left PFC patients]. The lack of a consensus among these studies might arise from a number of factors. First, reliance on subjective reports of recollection and familiarity may be complicated by the metamemory deficits in frontal patients [39]. Of note, different measures of familiarity were used in different studies (i.e., 'know' responses versus independence remember/know estimates of familiarity, see Ref. [40]), complicating comparison across studies. Second, the use of intentional encoding conditions [33,34] may lead to different results than incidental encoding [[38]; see also Ref. [35]]. In the former, recognition impairments may be the result of impairments at strategic encoding as well as impairments at retrieval, whereas in the latter case, deficits are likely to be primarily at retrieval. Memory deficits in frontal patients are reduced when encoding conditions are incidental or constrained [e.g., Refs. [41,42]], so it is possible that this contributes to the discrepancies between studies. Finally, high levels of performance in the ROC study [38] complicate the interpretation of those results, because ceiling effects can reduce the reliability of the estimates of recollection and familiarity [15].

The aim of the current study was to use receiver operating characteristics to investigate whether recollection, familiarity, or both are impaired in patients with lesions to the lateral prefrontal cortex. Incidental encoding was used to reduce demands on strategic processing at encoding, and memory was examined at two levels of performance (following shallow and deep encoding) to determine if the memory deficit generalizes across memories of different strength.

1. Method

1.1. Participants

Thirteen patients with unilateral prefrontal cortex lesions (7 left, 6 right) (mean age = 63.4 years, SD = 12.1) and 26 age-matched control participants (mean age = 62.9 years, SD = 11.2) took part in the experiment. Patient characteristics and neuropsychological test scores are shown in Table 1. Each patient was yoked to two age-matched controls. The average age of patients and controls was not different, $t < 1$. However, left LPFC patients ($M = 57.7$ years, SD = 11.0, $n = 7$) were younger on average than right LPFC patients ($M = 70.0$ years, SD = 10.5, $n = 6$), and this difference approached significance, $t(11) = 2.06$, $p = .06$. The control groups for the left and right patients also differed in age (left control group $M = 57.5$ years, SD = 11.0, $n = 14$; right control group $M = 69.1$ years, SD = 9.2, $n = 12$), and this difference was significant, $t(24) = 3.04$, $p = .006$. For this reason, age was used as a covariate in initial analyses, but follow-up tests did not use age as a covariate if there were neither main effects of age nor any interactions. The education levels of the patients ($M = 15.7$ years, SD = 3.6) did not differ from that of the controls ($M = 14.7$ years, SD = 1.84; $t(32) = 1.07$, $p = .29$). Left and right hemisphere patients also did not differ in education, $t < 1$.

Patients were recruited from the Veteran's Administration Northern California Health Care System (VANCHCS) in Martinez, CA and other participating hospitals and clinics. Patients were included if they were at least 6 months post-cerebral vascular accident and had no history of any other medical, neurological or psychiatric disorder. None of the patients were aphasic. The lesions for all patients were the result of middle cerebral artery infarcts. The lesions were centered in the lateral PFC encompassing both dorsolateral PFC (DLPFC; Brodmann's areas (BA) 9 and 46) and ventrolateral PFC (VLPFC; BA 44, 45 and 47) sub-regions with varying degrees of damage in BA 6, 8, and 10. Note that every patient had damage to at least one DLPFC region (BA 9 and 46) and only four patients had damage that did not include at least one VLPFC region (BA 44, 45, and 47). Group lesion overlaps are shown in Fig. 1a for the left LPFC group and Fig. 1b for the right LPFC group. The control participants were recruited from the Davis, Sacramento, and San Francisco Bay Area communities, and they had no history of neurological or psychiatric disorders. Participants were paid for participation and signed consent statements approved by the Institutional Review Boards of the University of California, Davis, the University of California, Berkeley, and the Veterans Administration Research Service.

1.2. Materials

Four-hundred and eighty nouns, adjectives, and verbs were selected from the Toronto word pool. The words ranged from 3 to 7 letters in length ($M = 5.4$, SD = 1.3) and from 1 to 3 syllables. Kucera–Francis frequency [43] ranged from 11 to 39 ($M = 20.7$, SD = 8.3). The words were randomly divided into two sets to serve in sessions 1 and 2. Each set was randomly divided into three lists. List 1 served as the first study list, list 2 served as the second study list, and list 3 served as non-studied lure items. The test list consisted of a random mixture of all the items from the three lists.

1.3. Design and procedure

Four PFC patients were tested in two 1-h sessions, and the remaining nine patients participated in one 1-h session. Controls yoked to the patients were matched to the patients for number of trials. Participants heard one list of words under deep encoding conditions (i.e., make an abstract/concrete judgment about each word), and then a second list of words under shallow encoding conditions (i.e., count the number of syllables in each word). For participants who took part in two sessions, the order of the encoding conditions was reversed for the second session. Participants were then read a test list and were required to make recognition memory judgments using a 6-point confidence scale from 'certain it was new' (1) to 'certain it was old' (6). The study and test phases were participant-paced. The participants responded verbally and the experimenter recorded their responses. Participants were instructed to spread their responses across the whole range from 1 to 6, and were reminded of this after they made their first few responses. Pilot studies with healthy controls suggested that these instructions were necessary in order to avoid having participants use only high-confidence or low-confidence responses. Failure to use the entire range of response confidence would lead to ROCs in which the points were closely clustered together, thus making the assessment of the function difficult.

2. Results

The mean proportion of responses in each confidence bin are shown separately for each of the patient and control groups in Table 2. In order to estimate the contributions of recollection and familiarity to recognition performance, confidence responses were used to plot receiver operating characteristics for each patient and control. The proportion of correct recognitions (hits) was plotted