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Case Study

The Medial Temporal Lobe Supports Conceptual Implicit Memory

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SUMMARY

The medial temporal lobe (MTL) is generally thought to be critical for explicit, but not implicit, memory. Here, we demonstrate that the perirhinal cortex (PRc), within the MTL, plays a role in conceptually-driven implicit memory. Amnesic patients with MTL lesions that converged on the left PRc exhibited deficits on two conceptual implicit tasks (i.e., exemplar generation and semantic decision). A separate functional magnetic resonance imaging (fMRI) study in healthy subjects indicated that PRc activation during encoding of words was predictive of subsequent exemplar generation. Moreover, across subjects, the magnitude of the fMRI and behavioral conceptual priming effects were directly related. Additionally, the PRc region implicated in the fMRI study was the same region of maximal lesion overlap in the patients with impaired conceptual priming. These patient and imaging results converge to suggest that the PRc plays a critical role in conceptual implicit memory, and possibly conceptual processing in general.

INTRODUCTION

Many theories of human long-term memory assume that explicit memory for prior events relies on the medial temporal lobe (MTL), which includes the hippocampus as well as the entorhinal, perirhinal (PRc), and parahippocampal (PHc) cortices. In contrast, implicit memory, which is measured in tasks where experience with a prior item facilitates the subsequent identification or production of that item, is thought to rely on associative cortical regions outside the MTL (Gabrieli, 1998; Schacter et al., 2000; Squire, 2004). Implicit memory effects can emerge as a byproduct of reprocessing the perceptual or conceptual aspects of an item and thus psychologists have distinguished between perceptually- and conceptually-driven priming effects. In general, studies have shown that the MTL is not critical for priming on perceptually-driven implicit memory tests (e.g., study ‘‘windsurfer,’’ then complete the word fragment ‘‘w_n__ur__r’’ at test) (Roediger and McDermott, 1993; Schacter and Buckner, 1998). Amnesic patients with MTL damage and who are impaired on explicit memory tests perform normally on perceptual implicit memory tests like word fragment completion (Blaxton, 1992; Cermak et al., 1988; Graf et al., 1984; Hamann and Squire, 1997), and neuroimaging studies have indicated that explicit memory is associated with MTL activation, whereas perceptual implicit memory is associated with activity in areas linked to stimulus identification such as the extrastriate cortex (Schacter et al., 1996; Schott et al., 2006).

It is less certain whether the MTL plays a critical role in conceptual forms of implicit memory. In conceptual implicit tests, prior processing of an item is found to facilitate performance on a task in which conceptual retrieval cues are provided (i.e., study ‘‘windsurf,’’ then generate an example of ‘‘a sport’’ at test). In behavioral experiments, conceptual implicit memory and familiarity-based recognition memory judgments are sensitive to the same kinds of manipulations (for a review, see Yonelinas, 2002), and several neuroimaging studies have demonstrated that familiarity-based recognition is supported by the PRc (for a review, see Eichenbaum et al., 2007). Although neuroimaging methods have not yet been used to study conceptual implicit memory in tasks like exemplar generation, imaging data indicate that PRc activity may be modulated by repeated semantic processing of the same item (O’Kane et al., 2005; Voss et al., 2009). Moreover, patients with damage to the PRc are impaired in their ability to make fine semantic discriminations between objects (e.g., tiger or lion) and PRc activation in healthy participants is increased when they make these kinds of semantic discriminations (Moss et al., 2005; Tyler et al., 2004). Furthermore, patients with semantic dementia have deficits in semantic processing, and this is sometimes accompanied by damage to the PRc (Davies et al., 2004, 2005). These findings suggest the possibility that the PRc contributes to conceptual processing, and therefore may also support conceptual implicit memory.

Here, we report three experiments testing the hypothesis that the PRc is critical for conceptual implicit memory. In experiments 1 and 2, we assessed amnesic patients and healthy controls on two conceptual implicit memory tasks, category exemplar

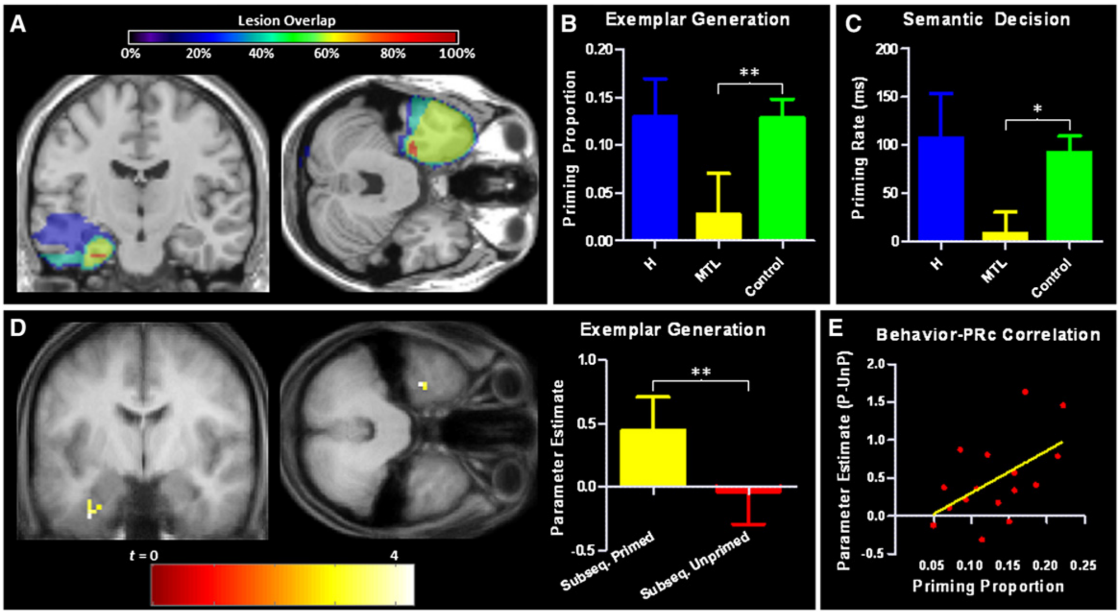

Figure 1. Conceptual Implicit Memory Performance and the PRc

(A) Lesion reconstruction overlaps of the MTL patient group consisting of left posterior cerebral infarct and temporal lobectomy patients. There was a region of maximum overlap in the left PRc.

(B) Category exemplar generation priming, measured as the proportion of old items produced minus the proportion of baseline items produced, for the hypoxic (H), medial temporal lobe (MTL), and control groups. Priming scores indicated that the MTL group had a significant deficit in conceptual implicit memory ($p < 0.05$), whereas performance in the H group was equivalent to that of the controls.

(C) Semantic decision priming, measured as the response time to make correct semantic decisions to repeated, compared to new, items, for the H, MTL, and control groups. Comparable conceptual priming effects were observed in the controls and the H group, but the MTL group was significantly impaired relative to controls ($p < 0.05$, one-tailed).

(D) Activation within the PRc region of interest found to be related to conceptual implicit memory. A cluster of voxels in the left PRc exhibited significantly greater activation for subsequent conceptually primed than unprimed words.

(E) The relationship between activity in the left PRc cluster and the magnitude of the behavioral priming effects in the exemplar generation task. Greater activity in the PRc was related to greater conceptual priming ($p < 0.05$). P = primed; UnP = unprimed.

generation and semantic decision, respectively. In the exemplar generation experiment, subjects encoded words and then were required to generate examples of semantic categories with the first words that came to mind. In the semantic decision experiment, subjects made speeded size judgments for words and pictures in the study phase then made similar judgments to repeated and novel items in the test phase. In experiment 3, we scanned healthy young adults while they encoded a list of words, and we subsequently tested conceptual (i.e., exemplar generation) and perceptual (i.e., fragment completion) implicit memory. The results showed that activation in the left PRc predicted subsequent conceptual implicit memory performance, and this region overlapped with the region of maximal lesion overlap in MTL patients with conceptual implicit memory impairments. Together, these results indicate that regions in the MTL, particularly the PRc, are critical for conceptual implicit memory.

RESULTS

Experiments 1 and 2—Conceptual Implicit Memory in Amnesia

To investigate the effects of MTL damage on conceptual implicit memory, we first examined performance on a category exemplar generation task in five patients with extensive damage to the left MTL (MTL group), four hypoxic patients (H group), and 22 age matched controls. The MTL group consisted of left posterior cerebral infarct and temporal lobectomy patients. Lesion reconstructions of computed tomography (CT) and magnetic resonance imaging (MRI) scans of the patients revealed that the region of greatest overlap was in the PRc (Figure 1A). This region was affected in four of the five subjects. The H group consisted of hypoxic patients with explicit memory deficits that were comparable to those of the MTL group (e.g., 74 and 73, respectively, on the Wechsler Memory Scale-Revised [WMSr] delayed memory subscales). Additionally, as reported in Yonelinas et al. (2002), both the H and MTL groups were impaired at recollecting qualitative details of prior study events, but only the MTL group exhibited impaired familiarity-based recognition. Lesion reconstructions could not be obtained in the hypoxic patients because of implanted defibrillators, but mild hypoxia is expected to lead to relatively selective damage to the hippocampus (e.g., Rempel-Clower et al., 1996).

After encoding a list of words by making pleasantness or syllable judgments, subjects were presented with 36 category cues, and asked to quickly provide the first five exemplars of the given category that came to mind. Twenty-four of the

Table 1. Mean Proportion of Target Items Generated by Group and Condition with Standard Deviations in Parenthesis on the Category Exemplar Generation Task for Patients and Controls

	Encoding Condition		
Group	Shallow	Deep	New
H	0.20 (0.04)	0.32 (0.06)	0.13 (0.08)
MTL	0.15 (0.01)	0.20 (0.10)	0.15 (0.06)
Control	0.26 (0.07)	0.32 (0.10)	0.16 (0.06)

H: hypoxic group; MTL: medial temporal lobe group.

category cues corresponded to previously studied exemplars. The remaining 12 category cues had no relationship to the studied items and were included to estimate the baseline generation rates in the absence of conceptual priming. Priming scores were collapsed across encoding condition (pleasantness/syllable judgment) because it did not interact with group (i.e., in all three groups priming was greater in the deep encoding condition) (Table 1). The three groups did not differ with respect to the proportion of baseline items produced ($F[2, 28] = 0.57$). Because of this, priming was measured as the proportion of old items produced minus the proportion of baseline items produced (Figure 1B). Planned contrasts indicated that the priming effects were significant in the H ($t[3] = 3.39$, $p < 0.05$), and control ($t[21] = 6.48$, $p < 0.01$) groups, and not significant in the MTL group ($t[4] = 0.53$). Furthermore, the MTL group was significantly impaired in conceptual priming compared to controls ($t[25] = 2.19$, $p < 0.05$), whereas there were no significant differences between the H group and controls ($t[24] = -0.28$). A direct comparison of the two patient groups showed that the priming effects were marginally smaller in the MTL group compared with the hypoxic group ($t[7] = 1.74$; $p = 0.06$, one-tailed). In sum, the results indicate that priming on conceptual implicit memory tests is not significantly affected by hypoxia, but damage to the temporal lobe regions surrounding the hippocampus (i.e., the PRc) does significantly reduce conceptual priming.

In order to test the generalizability of our results to other conceptual implicit memory tests, we investigated whether our findings would replicate using a semantic decision task. We compared semantic decision priming in the same MTL, H, and control groups as described above, except that the two left posterior cerebral artery infarct patients were not included in the MTL group because they could not easily complete the visual word reading task used in the current experiment. In the study phase, participants made speeded size judgments for words and pictures and then made similar judgments to repeated and novel items in the test phase. On average, patients and controls made similar percentages of errors at test (i.e., an incorrect decision about the relative size of an item compared to a shoebox); ~10% of all responses were incorrect. Only correct decisions that did not exceed two standard deviations (SD) from the participant's mean reaction time (RT) within each study-test condition were included in the analysis, resulting in the elimination of ~5% of the total number of responses for each group. Priming scores were collapsed across the study-test conditions as they did not interact with group (Table 2). The three groups exhibited equivalent RTs to new items ($F[2, 26] = 1.21$, $p > 0.05$), thus, similarly to the first experiment, priming scores were calculated as the difference in RT for novel (i.e., baseline) compared to repeated items (Figure 1C). Planned contrasts indicated that the priming effects were marginally significant in the H group ($t[3] = 2.32$, $p = 0.05$, one-tailed), significant in the control group ($t[21] = 5.46$, $p < 0.01$), and not significant in the MTL group ($t[2] = 0.40$). Importantly, the MTL group was significantly impaired in conceptual priming compared to controls ($t[23] = 1.78$, $p < 0.05$, one-tailed), whereas the H group did not perform differently from the controls ($t[24] = -0.33$). Moreover, the priming scores were marginally smaller in the MTL group relative to the hypoxic group ($t[5] = 1.71$; $p = 0.07$, one-tailed). Consistent with the exemplar generation priming results, semantic decision priming was intact in H patients, but significantly impaired in MTL patients.

The results from these two experiments demonstrate that conceptual priming can be consistently impaired in amnesia. These impairments, however, do not generalize to all amnesic patient groups. Hypoxic patients showed no indication of impairment in the exemplar generation or semantic decision priming tasks, whereas patients with extensive damage to the MTL, with the greatest amount of lesion overlap in the PRc (Figure 1A), exhibited significant impairments on both implicit tasks. Although these results implicate the PRc as a critical structure in conceptual implicit memory tests, in human lesion patients it is possible that the observed deficits may have been produced by undetected damage to other brain regions. Additionally, although most of the patients in the MTL group had documented damage to the left PRc, an examination of individual patient scores indicated that one of those patients did not appear to have a PRc lesion and yet still exhibited a low conceptual priming score. (The difference in the conceptual priming scores between the control and MTL groups in experiment 1 was medium [Cohen's $d = 0.55$] when this patient was removed; it was large [Cohen's $d = 0.87$] with this patient included.) To

Table 2. Mean RTs by Group and Condition with Standard Deviations in Parenthesis on the Semantic Decision Task for Patients and Controls

	Study → Test Condition					
Group	Pic. → Pic.	Pic. → Word	Word → Pic.	Word → Word	New Pic.	New Word
H	744.25 (64.98)	890.75 (111.30)	810.50 (53.92)	880.50 (141.37)	898.50 (179.47)	978.75 (112.92)
MTL	728.67 (149.49)	763.33 (196.02)	724.67 (84.61)	719.00 (120.02)	751.67 (104.16)	733.33 (100.38)
Control	686.91 (128.43)	796.86 (118.36)	743.77 (149.60)	772.00 (183.92)	831.05 (184.61)	853.82 (187.15)

H: hypoxic group; MTL: medial temporal lobe group; Pic: picture; RTs: reaction times.

further verify that the PRc is critically involved in conceptual implicit memory we next conducted a neuroimaging study on healthy individuals to determine if neural activity in the PRc is related to implicit memory.

Experiment 3—fMRI Activity Related to Conceptual Implicit Memory Encoding

Seventeen healthy participants were scanned while they encoded words by making pleasantness judgments for each item. Afterward, they were asked to complete a conceptual implicit memory test (i.e., category exemplar generation) to determine whether activity in the PRc during encoding was predictive of priming on the implicit test. Participants were then also given a perceptual implicit memory test (i.e., word fragment completion) in order to determine whether the regions involved in conceptual implicit memory might also be important for perceptual implicit memory. Priming effects were measured as the proportion of old items produced minus the proportion of baseline items produced. In the exemplar generation task, subjects were presented with 42 category cues at test (28 studied, 14 baseline) and asked to generate five exemplars per category. The mean priming score was 0.13 (SD = 0.05), which was significant ($t[15] = 10.10$, $p < 0.001$) and comparable to that observed in the controls in experiment 1. In the fragment completion test, subjects were presented with a total of 210 word fragments (140 studied, 70 baseline). The priming effect was 0.14 (SD = 0.05) and this priming effect was also significant ($t[16] = 11.55$, $p < 0.001$).

We first tested the a priori prediction that activation in the PRc would be increased for studied items that were subsequently produced in the exemplar generation test (i.e., primed) compared to those that were not produced (i.e., unprimed). As shown in Figure 1D, this contrast revealed a cluster of suprathreshold voxels in the left PRc (Montreal Neurological Institute [MNI] coordinates: $x = -33$, $y = -9$, $z = -36$ mm; $t[15] = 4.29$), indicating that it was involved in conceptual implicit memory. Importantly, this activation was in the same region as the MTL patient lesion reconstruction overlap (Figures 1A and 1D). No regions within the PRc showed less activation for subsequently primed items than for subsequently unprimed items.

To further examine the relationship between PRc activation and conceptual priming, we tested whether individual differences in functional magnetic resonance imaging (fMRI) subsequent priming effects (i.e., the difference in PRc activation between subsequently primed and unprimed items) were related to individual differences in the magnitude of behavioral conceptual priming effects. Activation in the left PRc was positively correlated with the magnitude of the behavioral priming effects ($r = 0.56$, $p < 0.05$), indicating that participants with larger subsequent priming effects in PRc during encoding exhibited larger behavioral priming effects (Figure 1E).

Additionally, an exploratory whole brain analysis was conducted to determine if there were regions outside the PRc that were also involved in conceptual implicit memory. Regions showing greater activation for subsequently primed compared to subsequently unprimed items included the right superior temporal gyrus (MNI coordinates: $x = 39$, $y = -51$, $z = 9$ mm; $t[15] = 4.60$), the right cerebellum ($x = 36$, $y = -63$, $z = -36$ mm; $t[15] = 5.22$), and the right thalamus ($x = 18$, $y = -24$, $z = 9$; $t[15] = 4.37$). No region showed less activation for primed compared to unprimed items. Unlike the PRc activation, none of these regions were significantly correlated with behavioral priming scores. However, direct comparisons indicated that these differences in correlations were not statistically significant.

Lastly, in order to determine whether the PRc is involved in perceptual forms of implicit memory, we examined whether PRc activation was related to subsequent performance on the fragment completion test. There were no regions within the PRc showing significant differences between subsequently primed and unprimed items. An exploratory whole brain analysis revealed a significant increase in activation in the left superior temporal gyrus for primed compared to unprimed items (MNI coordinates: $x = -51$, $y = -54$, $z = 18$ mm; $t[16] = 4.92$).

DISCUSSION

We conducted two experiments with amnesic patients and one fMRI study in healthy participants to test the hypothesis that the PRc plays a critical role in conceptual implicit memory. The results showed that patients with extensive MTL damage that converged in the PRc showed severe conceptual priming impairments relative to controls. In a separate fMRI experiment in healthy subjects, we found that PRc activity was increased during encoding of items that were subsequently produced in an exemplar generation test than those that were not, and there was a direct relationship between the PRc activity and the individual differences in conceptual priming effects. No relationships were observed between PRc activity and perceptual priming, suggesting that the observed PRc activity was specifically related to encoding in a conceptual implicit memory task. Thus, the patient and fMRI studies provided converging evidence to suggest a vital role for the left PRc in conceptual implicit memory.

The results from the present studies help to explain some discrepancies in the existing lesion literature on implicit memory. Various studies have reported evidence for preserved conceptual priming in amnesic patients in tasks like exemplar generation (Keane et al., 1997; Graf et al., 1985; Levy et al., 2004), whereas others have found evidence for a deficit (Blaxton, 1992; Cermak et al., 1988; Cermak et al., 1998; Cermak and Wong, 1998; Keane et al., 1997; Vaidya et al., 1996). However, many of these studies included a mixture of patients with damage to different MTL regions, which could account for the variable outcomes. Memory impairments seen in patients suffering from mild hypoxia (that can selectively affect the hippocampus) are quite different from those seen in patients with damage to the surrounding PRc and PHc (e.g., Yonelinas et al., 2002). Prior studies have found that conceptual priming is intact in amnesic patients with relatively selective hippocampal damage (Graf et al., 1985; Levy et al., 2004), whereas studies of patients with more extensive MTL damage reported impaired conceptual implicit memory (Blaxton 1992; Cermak et al., 1988). One exception is a study that reported normal conceptual priming effects in two patients with extensive MTL damage (Levy et al., 2004). However, the baseline level of performance in these patients was impaired relative to controls, which would be expected to artifactually inflate the priming scores of those patients (Ostergaard, 1999).

The present results are inconsistent with current theories of memory that assume that the MTL supports declarative but not nondeclarative memory (Squire, 2004); or that it supports episodic but not semantic memory (Schacter et al., 2000). More specifically, the results suggest that regions in the MTL, such as the PRc, contribute to normal performance on at least some types of implicit memory measures. The current results converge with other studies that have suggested that the MTL may contribute to implicit expressions of memory. For example, the MTL has been implicated in contextual cueing tasks (e.g., Chun and Phelps, 1999; Manns and Squire, 2001; Preston and Gabrieli, 2008), eye-movement based expression of relational memory (e.g., Ryan et al., 2000), transitive inference tasks (e.g., Greene et al., 2006), and measures of trace conditioning (e.g., Buchel et al., 1999; Cheng et al., 2008; McGlinchey-Berroth et al., 1997).

That said, one might question whether explicit memory processes such as conscious recollection or familiarity might have been related to the involvement of the PRc in conceptual implicit memory. A number of factors rule against the possibility that PRc involvement in conceptual implicit memory tests was related to recollection. First, the conceptual implicit memory tasks were designed to avoid the contaminating effects of explicit retrieval strategies. That is, both priming tasks were speeded to reduce the likelihood that recollection contributed to performance. Moreover, we found that PRc activation was correlated with subsequent conceptual priming even after removing subjects who claimed to use explicit retrieval strategies. Finally, numerous studies have demonstrated that the hippocampus, rather than the PRc, is necessary for recollection (Eichenbaum et al., 2007). If conceptual priming reflected the contribution of explicit recollection, then the amnesic hypoxic patients should have been impaired relative to the controls, and there was no evidence for any such impairment.

Although it is unlikely that conscious recollection contributed to the association between PRc and conceptual priming, it is possible that the same processes that drive familiarity-based recognition could have supported conceptual priming. Indeed, the MTL patients who exhibited conceptual implicit memory deficits in the current experiments were also shown to exhibit familiarity-based recognition deficits (Yonelinas et al., 2002). Furthermore, the present fMRI study found that left PRc activation during encoding was predictive of conceptual priming, and other fMRI studies of explicit memory have indicated that encoding activity in the left PRc was predictive of subsequent familiarity-based recognition memory (Davachi et al., 2003; Haskins et al., 2008; Kirwan et al., 2008; Ranganath et al., 2004). These results are consistent with findings that suggest that familiarity and conceptual implicit memory rely on the same underlying mechanisms (Verfaellie and Keane, 2002; Wagner and Gabrieli, 1998; Wagner et al., 1997; Yonelinas, 2002). Future research will be needed to investigate the role of the PRc in conceptual processing and how it relates to both familiarity-based recognition and conceptual implicit memory.

As noted earlier, there is an emerging body of evidence to suggest that the PRc may contribute to high level conceptual processing, and conceptual priming may be a byproduct of plasticity in PRc and other regions that occurs during processing of the conceptual features of an item. This account is broadly consistent with results from fMRI studies that showed reduced PRc activity during semantic judgments to repeated, relative to novel, words (O'Kane et al., 2005; Voss et al., 2009). Furthermore, semantic dementia patients with PRC damage have deficits in semantic processing (Davies et al., 2004; Davies et al., 2005), and the PRc appears to be necessary for making fine grained semantic discriminations (Moss et al., 2005; Tyler et al., 2004). Recent findings also indicate that the PRc may be critical for integrating cross-modal (e.g., visual and auditory) information into abstract and complex object-level representations (Holdstock et al, 2009; Taylor et al, 2006; Taylor et al., 2009). Additionally, recent work has indicated that the PRc supports high-level item representations that are important for the perception and short term maintenance of stimuli (e.g., Bussey and Saksida, 2007). Therefore, the PRc may be responsible for the integration of multiple item features including semantic information. During encoding, high level conceptual and semantic representations may be activated, and experience-dependent strengthening of these representations could lead them to be more accessible (i.e., easier to generate) at test. Consistent with this idea, subjects in the current fMRI study that showed more PRc activity at encoding had greater conceptual priming scores. Moreover, this explanation is compatible with the notion that both conceptual implicit memory and familiarity-based recognition may be mediated by conceptual fluency (Rajaram and Geraci, 2000; Wagner et al., 1997; Wagner and Gabrieli, 1998; Yonelinas, 2002).

Before closing, it is important to highlight the point that, in addition to the PRc, several other brain regions also may contribute to conceptual processing and conceptual implicit memory. The region of highest lesion overlap in the MTL patient group was in the left PRc, but this group included patients with lesions to the inferior and lateral temporal lobe and the inferior occipital lobe, and the results do not rule out a role for these other regions in conceptual implicit memory. Additionally, the fMRI results also revealed that activation in the right superior temporal gyrus was related to subsequent conceptual priming, and work with Alzheimer's patients has implicated the entorhinal cortex as playing a potential role in conceptual implicit memory (Fleischman et al., 2005). Future work will be necessary to determine whether or how these other regions might contribute to conceptual processing and/or implicit memory.

EXPERIMENTAL PROCEDURES

Experiment 1

Participants

The participant groups included hypoxics (H), medial temporal lobe patients (MTL), and age-matched healthy controls. These groups were assessed in previous recognition memory studies that indicated that the H group exhibited deficits in recollection but not familiarity-based recognition, whereas the MTL group exhibited deficits in both recollection and familiarity (Yonelinas et al., 2002). The H group consisted of four patients who suffered a mild episode of hypoxia during cardiac arrest. Due to the presence of defibrillators, these patients could not be scanned in order to conduct volumetric analysis. However, volumetric imaging (Gadian et al., 2000; Hopkins et al., 1995;

Kartsounis et al., 1995; Press et al., 1989; Vargha-Khadem et al., 1997) and postmortem neuropathological analysis (Cummings et al., 1984; Rempel-Clower et al., 1996; Zola-Morgan et al., 1986) indicate that mild hypoxia leads to bilateral lesions that are primarily limited to the hippocampus.

The MTL group consisted of five patients with damage that included the left hippocampus and surrounding cortex. Two of these patients had infarctions of the left posterior cerebral artery, and three had undergone left temporal lobotomies for treatment of intractable epilepsy. The damage in the infarct patients included the hippocampus, fornix, posterior portion of the parahippocampal gyrus extending up to the posterior surface of the amygdala, and the surrounding fusiform and lingual gyri. The lobectomy patients underwent a standard on block anterior temporal lobe resection to remove the anterior 4.5 cm of the temporal lobe, including the anterior half of the hippocampus, the amygdala, and the anterior third of the parahippocampal gyrus. The subject's lesion location and extent, obtained from CT and MRI films, were transcribed by an experienced neurologist (Dr. Knight) onto an averaged template in MNI space using MRIcron (see Rorden et al., 2007). Individual and group lesion volumes, as well as a group lesion overlaps were also obtained using the program. Lesion reconstructions revealed a region of overlap in four out of five of the MTL patients in the anterior parahippocampal gyrus, most likely the PRc.

The patients scored normally on tests of intelligence (M = 99 and 102 for the H and MTL groups, respectively). Moreover on the WMSr they were normal on attention subscales (M = 97 and 91), but impaired on the delayed memory subscales (M = 74 and 73) (Wechsler, 1987). The ages (M = 54 and 48) and years of education (M = 14 and 15) of the patient groups were comparable. The control group consisted of 22 healthy, age-matched participants recruited from the communities of Davis and Sacramento, California. The control group had a mean age of 54.00 (SD = 6.96) and an education level of 15.05 years (SD = 1.59). The controls did not differ from the patient groups in age or education. All subjects were paid for their participation and all procedures were approved by the University of California, Davis Institutional Review Board.

Materials

For the category exemplar generation task, five exemplars from 36 different categories (Battig and Montague, 1969) were chosen as target stimuli (i.e., 180 target items). Exemplars ranged from the 4th to the 32nd most frequently occurring exemplars for a given category. Target exemplars were divided into three study lists with each list containing 60 exemplars from 12 different categories. One list was assigned to a shallow study condition, one list was assigned to a deep study condition, and one list was not studied (i.e., new). Study list assignment was counterbalanced across participants and words were randomized within each list so that no two exemplars from a given category occurred in succession. Fourteen additional items were selected to be used as buffer items. Two buffer items were added to the beginning of each study list, and two buffer items were added to the end of each study list.

Design and Procedure

Items were read aloud one at a time to each participant, and the experimenter recorded the responses. For the first 30 items, they were asked to decide how many syllables were in each word (shallow encoding condition). For the next 60 items, they were asked to make pleasantness ratings for each word (deep encoding condition). For the final 30 items, they were again asked to decide how many syllables were in the word (shallow encoding condition). The two encoding lists were divided in such a way to control for the average study-test lag in the two study conditions. After the study phase, participants were given a category exemplar generation task. For this task, participants were presented verbally with 36 category cues, and asked to quickly provide the first five exemplars of the given category that came to mind. All responses were made verbally and the experimenter recorded the responses. Participants were given 90 s to generate their responses for each category cue. The exemplars for the nonstudied category cues served as a measure of baseline performance in this task. After the exemplar generation task, the control participants were given a questionnaire to assess whether they utilized explicit strategies on the task (Bowers and Schacter, 1990). Few control participants adopted intentional retrieval strategies (i.e., 7 of 34), and priming effects did not significantly differ between those participants who did adopt intentional retrieval strategies and those who did not.

Experiment 2

Participants

The patients and controls were the same as those tested in experiment 1 except that the two left posterior cerebral artery infarct patients were not included in the MTL group because they were letter-by-letter readers and could not easily complete the visual word reading task used in the current experiment.

Materials

For the semantic decision task, 120 pictures from Snodgrass and Vanderwart (1980) and their corresponding names were selected as target items. Half of the stimuli represented items that were bigger than a shoebox and half that were smaller. Note that the objective size of objects is somewhat ambiguous, given that many objects can take on several different forms (e.g., the word "basket" represents an item that can be larger or smaller than a shoebox). Items were chosen for which agreement was reached by three independent raters (two of the authors, A.P.Y. and M.M.L., and a third rater). For each participant, 80 items were randomly selected to serve as study items, half of which were to be presented as pictures and half as words. The test list contained 120 items (i.e., 20 were pictures at study and test; 20 were words at study and test; 20 were pictures at study and words at test; 20 were words at study and pictures at test; 20 were pictures at test and were not studied; and 20 were words at test and were not studied). Additional items (Snodgrass and Vanderwart, 1980) were selected to serve as buffer items at the beginning of the study list (i.e., 15 items) and the test list (i.e., 5 items).

Design and Procedure

Stimuli were presented on a laptop computer and participants responded via computer-monitored response buttons. At study, participants were presented with a mixed list of 80 items, half of which were presented as words and half of which were presented as pictures. The question, "Is it bigger than a shoebox"? was printed below each item. Participants responded by pressing response buttons labeled "yes" and "no." The test was self-paced, but participants were told to respond as quickly and accurately as possible. They were then presented with a test phase that was identical to the study phase except that 120 items were presented, 80 of which were repeated from the study list (i.e., 40 of these items repeated in the same format as studied, and 40 items repeated in the opposite format as studied).

Experiment 3

Participants

Participants were 17 right-handed native English speaking healthy young adults (ages 19–30; 12 female) from the University of California, Davis and surrounding communities. One participant was excluded from analysis of the conceptual implicit memory test because they performed at chance on that task. All subjects were paid for their participation and all procedures were approved by the University of California, Davis Institutional Review Board.

Materials

For the category exemplar generation task, the materials were similar to those of experiment 1, except that 30 additional exemplars (i.e., six categories) were added, ten exemplars per list, for a total of 70 target exemplars per list. A word fragment completion task was used as a measure of perceptual implicit memory. In this task, participants are given perceptual (i.e., word fragments) rather than conceptual (i.e., semantic categories) cues at test. The words and their corresponding fragments were selected from Blum and Yonelinas (2001). There were a total of 210 words, and the length of the words ranged from five to eight letters. Similarly to the category exemplar generation task, lists were counterbalanced and participants studied two of the lists while the third list remained unstudied.

Design and Procedure

For the study phase, participants were presented with a list of words and were asked to make pleasantness judgments for each word (1 = "very unpleasant," 2 = "moderately unpleasant," 3 = "moderately pleasant," 4 = "very pleasant"). Participants made pleasantness judgments for two experimental runs while inside the MR scanner. The word lists were randomized and each word was shown for 850 ms followed by a fixation cross for 1150 ms. Between word presentations, participants were given zero to three trials of a baseline task in which they saw a single digit (1–9) for 850 ms followed by a fixation cross for 1150 ms and made odd/even judgments (Stark and Squire, 2001).

Trial sequences and timings were optimized for fMRI using the optseq2 algorithm.

Ten minutes after the scan session was completed, participants were given a category exemplar generation task. For this task, participants were presented verbally with 42 category cues, and asked to quickly provide the first five exemplars of the given category that came to mind. The category cues that contained unstudied exemplars served as a measure of baseline performance in this task. Participants were then administered the word fragment completion task. Word fragments were presented on a laptop computer and participants verbally completed the fragments as the experimenter recorded the responses. Participants were given 4 s to complete each fragment. The fragments from the nonstudied word list served as a measure of baseline performance in this task. Finally, as in experiment 1, participants were given a questionnaire to assess whether they utilized explicit strategies on the task. Four of seventeen participants reported using explicit strategies in the exemplar generation task whereas ten reported using explicit strategies in the fragment completion task. However, the use of explicit retrieval strategies did not noticeably alter the pattern of behavioral or imaging results. Removing subjects that reported using explicit retrieval strategies did not significantly change behavioral priming scores. Moreover, a left perirhinal activation that significantly correlated with subsequent priming scores was still found when including only the subjects that did not use explicit retrieval strategies.

fMRI Acquisition and Analysis

MRI data was acquired using a 3T Siemens Trio scanner. Functional images were acquired using a gradient echoplanar imaging (EPI) sequence (repetition time [TR] = 2000 ms, echo time [TE] = 25 ms, field of view [FOV] = 220 mm, matrix size = 64×64). Each experimental run consisted of 217 volumes, where each volume consisted of 34 axial slices, with a voxel size of $3.4375 \times 3.4375 \times 3.4$ mm. Additionally, high resolution T1 coplanar images were also acquired from each participant. The EPI data was preprocessed with Statistical Parametric Mapping 5 (SPM5) software. After the first seven scans of each experimental run were discarded, the data were slice-time corrected using sinc interpolation to account for timing differences in acquiring of adjacent slices, realigned using a six-parameter, rigid-body transformation, spatially normalized to the MNI template, resliced into 3 mm isotropic voxels, and spatially smoothed with an isotropic 8 mm full-width at half-maximum (FWHM) Gaussian filter.

Statistical analyses were performed in SPM5 using the general linear model. A high pass filter and grand mean scaling were applied to the data. Trials were first modeled with a first-level fixed effects analysis using a canonical hemodynamic response function. Contrast images of subsequent conceptually primed > unprimed and subsequent perceptually primed > unprimed words were created and modeled in a one-sample t test in a second-level random-effects analysis. Significant clusters of activation within the PRc were identified using a voxel-wise threshold of $p < 0.005$ and a cluster size of six contiguous voxels to correct for multiple comparisons. This threshold was determined using Monte Carlo analysis with the AlphaSim program in the AFNI software package on a mask of the PRc, defined anatomically as the PRc (Insausti et al., 1998) in at least half of the subjects (Devlin and Price, 2007). With these thresholds, the family-wise error rate was restricted to $p < 0.05$. Suprathreshold clusters of voxels in the PRc were used to define regions of interest that were interrogated in subsequent correlational analyses. An exploratory whole brain analysis was also conducted using a threshold of $p < 0.001$, uncorrected, and a cluster size of 20 contiguous voxels, to correct for multiple comparisons.

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