Familiarity and Conceptual Priming Engage Distinct Cortical Networks

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Familiarity refers to an explicit recognition experience without any necessary retrieval of specific detail related to the episode during which initial learning transpired. Prior experience can also implicitly influence subsequent processing through a memory phenomenon termed conceptual priming, which occurs without explicit awareness of recognition. Resolving current theoretical controversy on relationships between familiarity and conceptual priming requires a clarification of their neural substrates. Accordingly, we obtained functional magnetic resonance images in a novel paradigm for separately assessing neural correlates of familiarity and conceptual priming using famous and nonfamous faces. Conceptual priming, as shown by more accurate behavioral responses to strongly conceptually primed than to weakly conceptually primed faces, was associated with activity reductions in left prefrontal cortex, whereas familiarity was associated with activity enhancements in right parietal cortex for more-familiar compared with less-familiar faces. This neuroimaging evidence implicates separate neurocognitive processes operative in explicit stimulus recognition versus implicit conceptual priming.

Keywords: explicit memory, fMRI, functional magnetic resonance imaging, implicit memory, memory systems, neuroimaging

Introduction

Although familiarity and conceptual priming are distinct behavioral manifestations of memory, controversy surrounds the question of whether they are nonetheless subserved by identical neural populations. *Familiarity* occurs when a person recognizes that a stimulus or episode occurred previously, although it is not necessary for this recognition to be accompanied by retrieval of details concerning the initial experience (as in episodic *recollection*). As familiarity entails the conscious awareness of recognizing, it is an example of *explicit memory*. In contrast, *implicit memory* refers to a phenomenon where prior experience influences subsequent behavior without any necessary awareness of memory retrieval (Gabrieli 1998). *Conceptual priming* is a form of implicit memory tied to the conceptual meaning of the stimulus. It is often revealed by faster or more accurate behavioral responses in tests that indirectly provoke access to the primed information, as in the case of free-association and category-verification tests (Schacter and Buckner 1998).

A currently popular hypothesis posits that familiarity-based recognition is supported by the same neural processes that lead to conceptual priming (e.g., Jacoby 1991; Whittlesea and Williams 1998; Rajaram and Geraci 2000; Yonelinas 2002; Wolk et al. 2005). Consonant with this proposal, behavioral measures of familiarity and conceptual priming are often influenced in

a parallel way by various manipulations (e.g., both enhanced by semantically-deep encoding; reviewed in Yonelinas 2002). In addition, conceptual priming has been shown to enhance the bias to report familiarity-based recognition (Rajaram and Geraci 2000; Wolk et al. 2005).

However, neuropsychological observations indicate that familiarity and conceptual priming can be neuroanatomically dissociated, in that patients with amnesia can exhibit impaired familiarity (Knowlton and Squire 1995; Yonelinas et al. 1998; Khoe et al. 2000) and preserved conceptual priming (Graf et al. 1985; Vaidya et al. 1995; Keane et al. 1997; Levy et al. 2004). If familiarity indeed depends on the same neurocognitive events that underlie conceptual priming, then patients should exhibit either preservation in both or impairment in both. On the other hand, these neuropsychological results do not preclude the possibility that a causal relationship between familiarity and conceptual priming is operative in healthy brains but that these memory processes function differently in amnesic patients.

Direct comparisons between neural correlates of conceptual priming and explicit memory are thus needed, but have rarely been attempted (Donaldson et al. 2001; Voss and Paller 2006). The present study is the first to employ specific behavioral measures of both conceptual priming and familiarity, and to track both memory phenomena using measures of neural activity obtained during a single behavioral task. These neuroimaging results thus provide highly relevant evidence for determining if distinct neural events or the same neural events support these 2 different behavioral manifestations of memory.

Methods

Materials and Behavioral Paradigm

Visual stimuli consisted of 180 grayscale images of celebrity faces as well as 180 similar-format images of nonfamous individuals. Three written biographical cues were generated for each celebrity (as listed in Supplemental Table 1 of Voss and Paller 2006). One cue was always the name of the celebrity and the other 2 were relevant dramatic roles, song titles, film titles, political offices, and the like. For example, biographical cues for Harrison Ford were "Harrison Ford," "Indiana Jones," and "Han Solo," and for Madonna were "Madonna," "Like a Virgin," and "Like a Prayer."

The experiment comprised 4 distinct phases, as represented schematically in Figure 1 along with timing parameters. Phases 1–3 paralleled those in Experiment 3 of Voss and Paller (2006), except for small timing alterations made to facilitate functional magnetic resonance imaging (fMRI) analyses. Each stimulus in phases 2 and 4 was synchronized to the scanner's time of repetition, and order of trials was pseudorandomly selected to maximize the accuracy of hemodynamic response deconvolution. Whereas event-related potential (ERP) data were acquired during Experiment 1 of our previous study, the ERP experiment differed from the current design in that unprimed celebrities in phase 1 were presented along with biographical cues
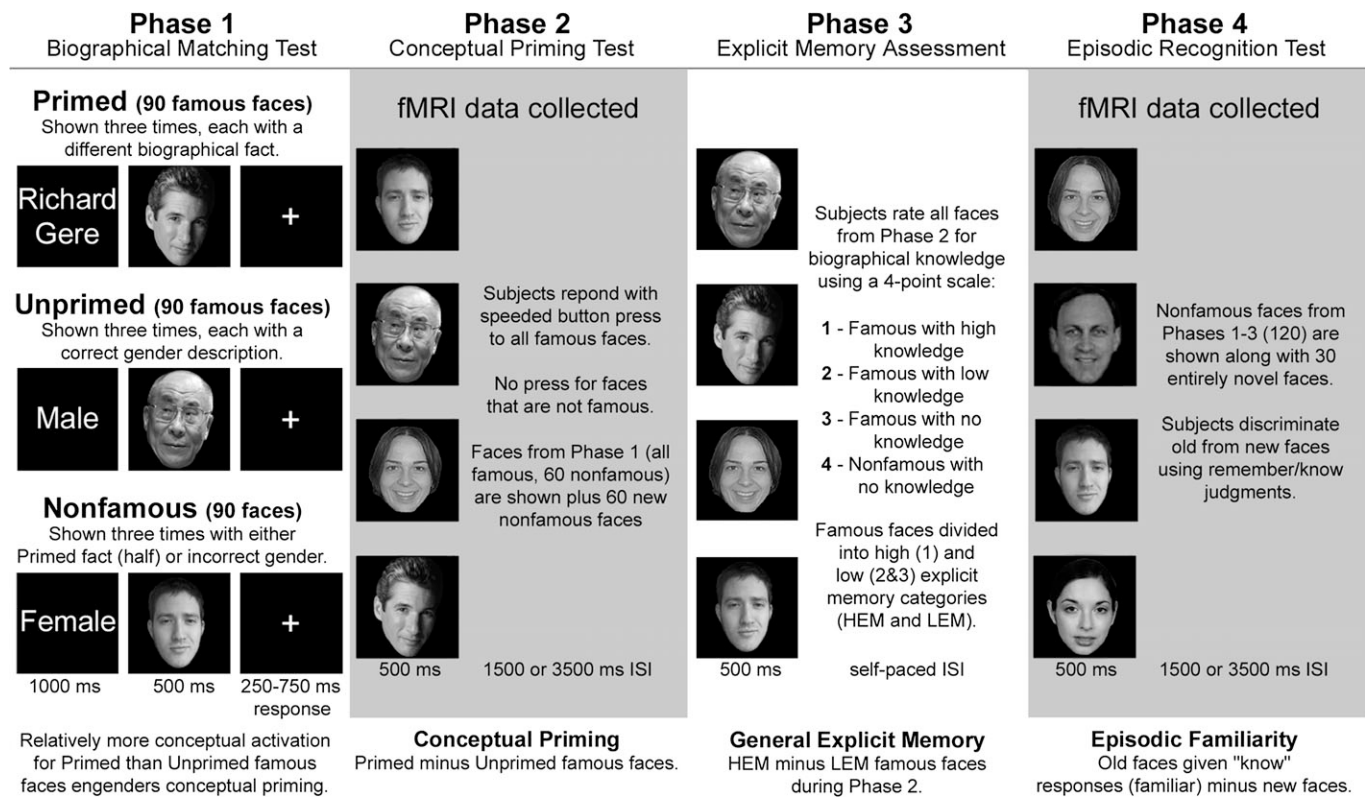
Figure 1. Schematic representation of the behavioral paradigm. The 4 experimental phases are depicted, showing the contrasts used to isolate neural correlates of 3 mnemonic phenomena—conceptual priming, general explicit memory, and episodic familiarity.

matching primed celebrities (see above) rather than the matching gender descriptions used here. The current design produced similar behavioral priming to that in the ERP design in our previous report (Experiments 1 and 3 of Voss and Paller 2006), and we therefore hypothesize that our ERP and fMRI findings will index similar neurocognitive operations.

Phase 1: Biographical Matching Test
Outside the scanner, subjects were cued to bring to mind specific conceptual information for primed famous faces but not unprimed famous faces. Primed famous faces (90) were preceded by a matching biographical cue. Unprimed famous faces (90) were not preceded by a matching biographical cue, but were instead preceded by an appropriate description of gender (either "male" or "female"). The famous faces assigned to primed and unprimed categories were counterbalanced across subjects. Nonfamous faces (90) were also presented, half with a randomly selected biographical cue matching a primed famous face and the other half with an incorrect gender description, such that the type of verbal cue was orthogonal to the famous/nonfamous dimension. Accordingly, some biographical cues, randomized across subjects, were presented on more than one occasion during phase 1, once with the appropriate primed famous face and once with a nonfamous face. Subjects responded to each face by pressing either a "match" or "does not match" button. Assuming correct responding, all famous faces would be endorsed with "match" responses such that subsequent priming differences for primed and unprimed faces could not be attributed to differential stimulus-response mapping. All nonfamous faces would be endorsed with "does not match" responses (nonmatching biographical cue or nonmatching gender), to balance against the large number of "match" responses.

Phase 1 was divided into 3 segments (without breaks), each face appearing once per segment. For primed faces, each matching biographical cue was used once per segment in randomized order. Faces were shown for equal duration in random order. The rapid sequence of stimuli and response demands served to greatly limit the extent to which subjects could retrieve information pertaining to

unprimed famous faces. This greater conceptual activation for primed compared with unprimed famous individuals allowed us to obtain measures of conceptual priming in the next phase of the experiment. Thus, behavioral measures in phase 1 were not intended to assess the immediate influence of cues on face processing; instead, in phase 2 we examined memory effects beyond the span of immediate memory. Subjects were positioned in the MRI scanner following phase 1.

Phase 2: Conceptual-Priming Test
Approximately 15 min after phase 1 ended, subjects viewed all 180 famous faces, 60 randomly selected nonfamous faces from phase 1 (half of which were initially presented with a gender cue and half with a primed celebrity biographical cue), and 60 novel nonfamous faces, in pseudorandom order. Subjects responded with a speeded button-press to each famous face and did not respond to nonfamous faces.

We hypothesized that facilitated responses to primed famous faces relative to unprimed famous faces would reflect conceptual priming. Although unprimed famous faces likely recruited some conceptual activation during phase 1, this was undoubtedly less than for primed faces. We used the term "unprimed" to indicate relatively low conceptual priming, not a total lack of priming. Some priming could also be expected from pre-experimental experiences and perhaps from biographical information for other celebrities, such as those who appeared in the same film. In short, the primed-versus-unprimed contrast is intended to focus on a relative difference in conceptual priming (high priming vs. low priming). Although other tests, such as the category-verification test, have typically been used to measure conceptual priming, judging whether a face is famous is a suitable task requirement, which is analogous to other conceptual-priming tasks because it involves access to pertinent conceptual information and does not make explicit reference to prior learning episodes. In this case, any of the biographical information selectively brought to mind in phase 1 could conceivably facilitate the decision in phase 2 that a corresponding face is famous. Importantly, explicit retrieval of phase 1 episodes was not required and would likely be counterproductive to speeded task performance if emphasized, in that retrieval of specifics

could slow decisions to the extent that such retrieval was effortful or distracting. Furthermore, we previously studied conceptual priming using highly similar task requirements, and ERP results showed no evidence that facilitated fame judgments for primed versus unprimed conditions were driven by explicit memory (Voss and Paller 2006).

The design also minimized the influence of 2 other forms of implicit memory on response differences between primed and unprimed famous faces. Perceptual priming was matched, given that each famous face appeared an equal number of times in phase 1 with comparable sensory processing. Differential elaborative processing due to task requirements would not be expected to influence perceptual priming for faces, given that exactly this outcome was found in a prior experiment with faces (Paller et al. 1999). In addition, response priming (Dobbins et al. 2004) was equivalent for primed and unprimed famous faces, because they were all endorsed with "match" responses during phase 1.

Phase 3: Explicit Memory Assessment
Immediately after phase 2, all faces from that phase were presented again in a different random order. Subjects rated each face using a 4-point scale (Fig. 1), indicating the extent to which each face was known. This measure provided an index of the amount of information that may have been available for incidental retrieval in response to each face during phase 2. This explicit retrieval potentially included multiple types of information: episodic and semantic information learned prior to the experiment as well as episodic and semantic information from phase 1 or phase 2. We reasoned that a different memory task requiring a specific assessment of only episodic information from phase 1 would not have been useful, because it was unlikely that we could prevent subjects viewing famous faces from retrieving the other types of information as well, even though not required by task instructions. Consequently, brain activity associated with explicit retrieval would potentially pertain to all these types of information together, and we would not have a corresponding behavioral index of the diverse types of retrieval likely to have occurred. Given that isolating episodic retrieval would be questionable, the behavioral assessment of general explicit memory in phase 2 was thus designed to potentially include all types of information that subjects would explicitly retrieve. Only famous faces correctly identified as famous in both phase 2 and phase 3 were included in fMRI analyses.

Phase 4: Episodic Recognition Test
A specific index of familiarity, as distinct from other explicit memory phenomena, was obtained immediately after phase 3. Subjects discriminated 120 nonfamous faces that appeared previously in the experiment (half during all previous phases, half during only phases 2 and 3) from 30 entirely novel nonfamous faces. Subjects responded to each face using 3 buttons corresponding to *remember*, *know*, and *new*. *Remember* responses indicated recognition that an item was old accompanied by retrieval of specific detail from prior episodes, whereas *know* responses indicated recognition that an item was old unaccompanied by any such detail. Remember and know responses are commonly used to index recollection and familiarity, respectively, during recognition testing (Yonelinas 2002).

Subjects
Behavioral and fMRI data were obtained from 11 right-handed, native speakers of English recruited from the Northwestern University community (6 female, ages 20–34), all with normal or corrected-to-normal vision. Data from an additional 4 subjects were excluded from all analyses. One excluded subject moved excessively in the scanner and 3 recognized <60% of celebrity faces during phase 2 of the experiment such that there were too few trials when famous faces were divided into separate explicit memory categories based on phase 3 ratings. All included subjects endorsed over 70% of the celebrity faces as famous with responses during both phase 2 and phase 3. All participants provided written, informed consent.

fMRI Parameters
During phases 2 and 4, fMRI data were collected using a Siemens, New York City, NY TRIO 3.0-T MRI scanner. Whole-brain gradient-recalled echo-planar images were obtained every 2 s (35 3-mm axial slices, 0-mm gap, repetition time = 2000 ms; echo time = 25 ms; flip angle = 80°; field-of-view = 22 cm; 64 × 64 acquisition matrix; voxel size = 3.44 × 3.44 × 3 mm, 522 volumes collected during phase 2 and 122 volumes during phase 4). Experimental stimuli were not presented during the first 10 volumes, when the scanner reached steady state, and these data were discarded. Following phase 4, high-resolution whole-brain structural images were collected to provide anatomical localization (3D magnetization prepared rapid gradient echo T_1-weighted scans, voxel size = 0.859 × 0.859 × 1 mm; 160 axial slices).

fMRI Data Analysis
AFNI software (Cox 1996) was used for data analysis. Preprocessing included coregistration through time for motion correction, removal of voxels with low signal (<30% of mean whole-brain signal) or erratic signal (>30% change over 1 volume), spatial smoothing (7-mm full width half maximum Gaussian kernel), coregistration with the structural image, and transformation to Talairach–Tournoux stereotactic space (MNI-305). Hemodynamic response deconvolution with a general linear model provided estimates of stimulus-locked neural activity, as quantified using average values from 5- to 9-s poststimulus, thus accounting for hemodynamic lag. Regions exhibiting group-level activation differences between experimental conditions were identified via a 2-pass random-effects analysis. For each experimental contrast, Monte Carlo simulations performed using AFNI/AlphaSim estimated the likelihood of detecting false positives over multiple voxel-wise comparisons. For an individual-voxel probability threshold of $P = 0.01$, we identified the voxel cluster-size threshold necessary to achieve an overall reliability threshold of $P = 0.01$ (cf. Forman et al. 1995). For each contrast, 30 000 simulation iterations were performed in which 2 suprathreshold voxels were considered contiguous if at least 1 vertex was touching. The most stringent resultant cluster-size threshold, 12 contiguous voxels, was applied to each contrast.

Results

Conceptual Priming for Famous Faces
Priming is often indexed by higher accuracy for primed relative to unprimed stimuli. In Experiments 1–3 of Voss and Paller (2006), we identified accuracy effects attributed to conceptual priming ranging from approximately 3–7% using designs paralleling the current design (identical priming task procedures were used in the previous Experiment 3; slightly modified priming procedures in previous Experiments 1 and 2). Here, primed famous faces were identified with greater accuracy than were unprimed famous faces during phase 2 (mean accuracy = 89.1% and 86.4%, respectively; $t(10) = 2.1$, $P = 0.03$, 1 tailed), providing a behavioral correlate of conceptual priming. Mean accuracy was significantly higher for primed versus unprimed famous faces ($t(35) = 6.2$, $P < 0.001$) when behavioral data from the present experiment were combined with behavioral data from our previous 3 experiments. In the current data, there was no evidence of a speed–accuracy tradeoff, as there was a nonsignificant trend for reaction times to primed famous faces to be faster than those to unprimed famous faces (mean reaction time = 704 and 713 ms, respectively; $t(10) = 0.5$, not significant [ns]). False alarms to nonfamous faces were made very rarely (mean = 3.2%, standard error [SE] = 2.7%). Our 3 previous experiments each identified robust evidence for conceptual priming as measured by enhancements of both reaction time and accuracy. We attribute the reduced magnitude of priming here to both the small sample size and the delay and interference caused by the transfer of subjects into the MRI scanner between phase 1 and phase 2. Priming effects often decline sharply as the retention delay increases (Gabrieli 1998; Schacter and Buckner 1998; but see Mitchell 2006), which could be especially prominent for

conceptual compared with perceptual priming. Furthermore, environmental context effects (Parker et al. 1999) would predict that a change in environment could also reduce priming. Although these measures of priming were marginal, conceptual priming was not absent altogether and still led to corresponding differences in neural activity. The fMRI contrast between primed and unprimed famous faces identified neural activity within the set of brain regions listed in Table 1A.

General Explicit Memory for Famous Faces

To identify neural correlates of general explicit memory retrieval likely to have occurred incidentally during phase 2, ratings made during phase 3 were used to classify phase 2 trials as either 1) famous faces provoking High Explicit Memory retrieval (HEM; response *1* on the 4-point scale; 45% [SE = 7%] of famous faces and 0% [SE = 0%] of nonfamous faces on average) or 2) as famous faces provoking Low Explicit Memory retrieval (LEM; response *2* or *3*; 46% [SE = 8%] of famous faces and 0.7% [SE = 0.6%] of nonfamous faces on average). On average, 9% (SE = 3%) of famous faces were rated as nonfamous (response *4*), whereas 98% (SE = 3%) of nonfamous faces were correctly classified. The mean response time was 1365 ms and nonsignificant repeated-measures analysis of variance main effects and interaction effects indicated that response times did not vary as a function of response type, face type (famous or not famous), or conceptual priming (primed/unprimed). The

mean percentage of ratings and reaction times for each face and response category are provided in Table 2. This general-explicit-memory contrast between HEM and LEM famous faces was found to be orthogonal to the conceptual-priming contrast, in that the primed and unprimed famous face categories included roughly equal numbers of HEM faces on average (52% of HEM faces were primed, SE = 5.1%; $t(10)$ = 0.5, ns for the number of HEM faces that were primed vs. unprimed). Furthermore, the percentage of primed versus unprimed famous faces did not differ significantly across all of the 4 rating levels ($F_{1,10}$ = 0.89, ns) or as a function of rating level ($F_{3,30}$ = 0.92, ns), indicating that priming did not influence explicit memory ratings. Neural activity identified by this general-explicit-memory contrast included responses within the set of brain regions listed in Table 1B.

Familiarity for Nonfamous Faces

During phase 4, subjects were significantly better than chance at discriminating incidentally encoded nonfamous faces from novel nonfamous faces (mean d' = 0.93, $t(10)$ = 7.9, P < 0.001). Familiarity often occurred in the absence of recollection, as an average of 81% (SE = 0.5%) of correct responses on old trials were *know* responses. The mean percentage of remember, know, and new responses for old trials was 13% (SE = 3%), 53% (SE = 4%), and 34% (SE = 4%), respectively, and for new trials 2% (SE = 1%), 30% (SE = 4%), and 68% (SE = 4%), respectively.

Table 1
Summary of regional activation clusters for each experimental contrast, including Broadmann area (BA), sign of the difference (+/−), hemisphere (left/right), centroid Talairach–Tournoux coordinates, volume, and mean statistical difference across the cluster

Experimental contrast	Sign	Hemisphere	Centroid coordinates			Volume (mm³)	t value
Region (BA)			x	y	z		
A. Conceptual-priming contrast: (primed − unprimed)							
SFG (8)	−	L	−16	38	48	391	3.7
IFG (45/47)	−	L	−50	19	3	203	3.5
Middle temporal gyrus (39/19)	+	L	−44	−74	16	1000	3.9
Posterior cingulate gyrus (31)	+	L	−8	−63	16	609	3.9
Fusiform/parahippocampal gyrus (19/37)	+	L	−27	−56	−6	422	3.6
Anterior cingulate gyrus (24)	+	L	3	21	9	234	3.9
B. General-explicit-memory contrast: (HEM − LEM)							
Inferior/superior parietal lobule (40/7)	+	R	43	−42	47	2527	4.2
Medial frontal gyrus (10)	+	L	−1	62	10	859	4.7
Posterior cingulate gyrus (31)	+	L	−6	−56	23	516	3.8
Inferior temporal gyrus (19)	+	L	−52	−72	−1	469	4.1
Angular gyrus (39)	+	L	−43	−70	27	297	4.0
C. Episodic-familiarity contrast: (know − new)							
Middle occipital gyrus (19)	−	L	−29	−63	3	967	4.6
Lingual gyrus (18)	−	L	−16	−73	−8	422	4.0
IFG (9)	−	R	25	20	−12	344	4.3
Inferior/superior parietal lobule (40/7)	+	R	35	−41	56	4446	4.7
SFG (6)	+	L	−6	7	51	781	4.4
Cingulate gyrus (18)	+	L	1	−28	27	656	3.9
IFG (9)	+	L	−44	10	29	250	4.0
D. General explicit memory minus conceptual priming: (HEM − LEM) − (primed − unprimed)							
IPL (40)	+	R	43	−40	48	1996	4.1
Paracentral lobule (5)	+	L	−6	−39	57	578	4.0
SFG (8)	+	L	−15	29	51	500	3.8
IFG (45/47)	+	L	−52	30	4	266	3.7
E. Episodic familiarity minus conceptual priming: (know − new) − (primed − unprimed)							
Medial frontal gyrus (10)	−	R	14	38	−10	641	3.9
Subcallosal gyrus (47)	−	R	20	19	−10	484	3.9
Lingual gyrus (19)	−	L	−26	−63	−1	344	4.0
Inferior/superior parietal lobule (40/7)	+	R	35	−39	57	4774	4.3
SFG (8)	+	L	−18	33	51	1185	3.8
Putamen	+	R	28	2	2	686	3.9
IFG (45/47)	+	L	−51	18	3	500	3.6

Note: For single subtractions (condition X minus condition Y), a positive sign indicates that condition X was greater than condition Y whereas a negative sign indicates that condition Y was greater than condition X. For double subtractions (contrast X minus contrast Y), a positive sign indicates that contrast X was more positive than contrast Y whereas a negative sign indicates that contrast Y was more positive than contrast X.

Table 2

Table 2
Mean rating percentages (%) and reaction times (RT) for primed and unprimed famous faces and repeated and novel nonfamous faces during phase 3, subdivided by category

| | HEM | | LEM | | | | Nonfamous | |
| | Rating 1 | | Rating 2 | | Rating 3 | | Rating 4 | |
	%	RT	%	RT	%	RT	%	RT
Famous								
Primed	47	1376	23	1255	22	1302	8	1433
Unprimed	44	1298	27	1572	20	1197	9	1371
Nonfamous								
Repeated	0	—	0	—	0.4[a]	1229	97[a]	1364
Novel	0	—	0	—	1[a]	1425	98[a]	1314

[a]Percent responses for nonfamous faces did not total 100 due to a failure to respond.

Response times varied as a function of response type and old/new status (interaction $F_{2,20} = 9.7$, $P = 0.001$), as remember responses to old faces were faster than responses in all other categories (all pairwise P's $\leqslant 0.001$), whereas other response categories did not differ significantly from each other (all pairwise P's > 0.14). The mean response time to old remember faces was 1117 ms, and the mean response time for all other categories together was 1587 ms. Corresponding neural correlates of familiarity were obtained by contrasting fMRI responses to repeated nonfamous faces given *know* responses versus new nonfamous faces given *new* responses. This episodic-familiarity contrast identified activity within the set of brain regions listed in Table 1C.

Isolating Familiarity within General Explicit Memory

In order to make comparisons between implicit and explicit memory within the same task, it was necessary to obtain neural correlates of both types of memory for the famous faces presented during the conceptual-priming test (phase 2). However, the general-explicit-memory contrast (HEM/LEM) made using fMRI data from phase 2 did not focus specifically on familiarity. Indeed, it may not be possible to prevent multiple explicit memory phenomena from being mobilized in response to images of such well-known people. We did not include a "process-pure" test of episodic familiarity based on phase 1 episodes because we reasoned that neural measures of familiarity would still be contaminated due to semantic retrieval of the wealth of celebrity-related knowledge previously learned by our subjects, even if the task only required episodic retrieval.

To overcome these challenges and identify neural correlates of familiarity, data from the general-explicit-memory contrast for famous faces (HEM/LEM, phase 2) and the episodic-familiarity contrast for nonfamous faces (old-know/new, phase 4) were pooled by selecting voxels that were jointly identified as significantly active by both contrasts. This was performed via a logical "AND" operation by selecting only those voxels, which were suprathreshold in both the HEM/LEM contrast and the familiarity contrast. Whereas these 2 contrasts identified activity related to some distinct mnemonic phenomena, both contrasts included activity related to familiarity. Moreover, these contrasts converged in that they both identified a set of voxels of significantly enhanced activity in right inferior parietal lobule (IPL, Fig. 2). This activation was thus taken as a neural correlate of familiarity within the general-explicit-memory contrast. No other convergent voxels were identified.
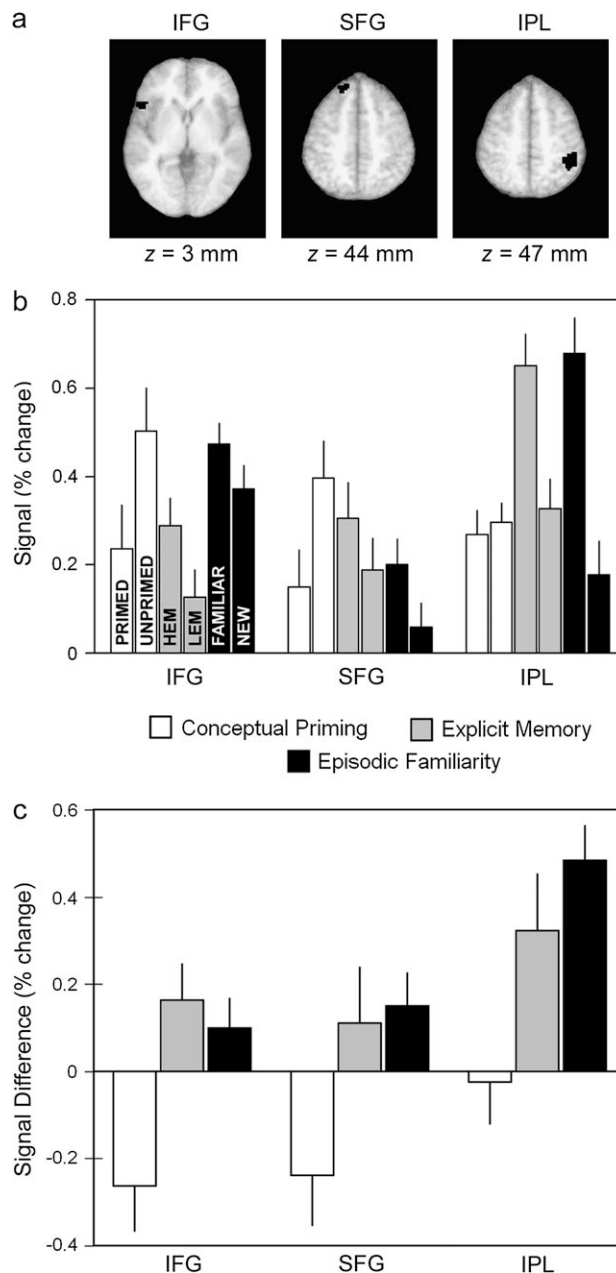

Figure 2. Double dissociation between fMRI correlates of conceptual priming and familiarity. (*a*) Three regions (black voxels) were identified via double subtractions between conceptual priming and general explicit memory and between conceptual priming and episodic familiarity. Regions of left SFG (BA 8) and IFG (BA 45/47) were also identified by the conceptual-priming contrast. The region of right IPL was also identified by both the general-explicit-memory contrast and the episodic-familiarity contrast (IPL, BA 40, centroid Talairach–Tournoux coordinates = 43 *x*, −42 *y*, 49 *z*, volume = 1203 mm³). (*b*) The average magnitude of the blood oxygen level–dependent (BOLD) response from 5 to 9 s for each experimental condition is shown averaged over these regions. (*c*) The double dissociation is apparent in the average differences between conditions that constituted the 3 experimental contrasts. Error bars indicate SE. The reported effects reflect signal enhancements or reductions in positive-going BOLD responses (estimated impulse response functions for each condition appear in Fig. S1).

Double Dissociation of Familiarity and Conceptual Priming

A double subtraction between the conceptual-priming contrast and the general-explicit-memory contrast indicated that conceptual-priming effects were significantly greater in

magnitude than explicit-memory effects in regions of left prefrontal cortex identified as the inferior frontal gyrus and the superior frontal gyrus (IFG and SFG, Fig. 2, Table 1D). These activations were also found in the conceptual-priming contrast (Table 1A), and were characterized by response reductions in both cases. Conversely, neural explicit-memory effects were greater in magnitude than conceptual-priming effects in a region of right IPL (Fig. 2, Table 1B). Specifically, the double subtraction identified response enhancements in a subset of IPL voxels that were attributed to familiarity within the general-explicit-memory contrast. To summarize this result, neural correlates of conceptual priming (prefrontal response reductions) and general explicit memory (parietal response enhancements) were dissociated for famous faces within phase 2, and results from the episodic-familiarity contrast for nonfamous faces within phase 4 showed that the explicit-memory effects in parietal cortex in phase 2 were likely associated with familiarity.

The same pattern of activity within spatially overlapping regions in IFG, SFG, and IPL was identified by a double subtraction between the conceptual-priming contrast for phase 2 and the episodic-familiarity contrast for phase 4 (Fig. 2, Table 1E). Thus, neural correlates of conceptual priming differed from those of episodic familiarity for nonfamous faces in the same manner as they differed from neural correlates of explicit memory for famous faces. Conceptual priming and familiarity were neurally distinct in 1) reliance on activity within separate anatomical regions, and 2) the polarity of relevant neural processing: activation reductions for conceptual priming in IFG and SFG, activation enhancements for familiarity in IPL.

Discussion

Measures of event-related hemodynamic responses revealed distinct neural substrates for conceptual priming and familiarity. Our novel experimental procedures employed direct observations of both memory phenomena in analyses of neuroimaging data from a single memory test, thus permitting novel comparisons between corresponding fMRI correlates. When neural correlates of familiarity and conceptual priming are obtained in separate tasks (Donaldson et al. 2001), differences in task factors could potentially have an undesirable influence on neural comparisons. The present tactics minimized that possibility. The double dissociation between neural correlates of familiarity and conceptual priming validates previous evidence (Donaldson et al. 2001; Voss and Paller 2006) that these manifestations of memory result from distinct neurocognitive events.

Conceptual priming for famous faces was associated with response reductions (less-positive responses for primed compared with unprimed faces) in 2 regions of left prefrontal cortex, IFG and SFG. Neural correlates of conceptual priming and explicit memory were dissociated via a double subtraction involving the conceptual priming and general-explicit-memory contrasts for famous faces. As summarized in Figure 2, conceptual priming was associated with response reductions in left prefrontal cortex (IFG and SFG), whereas explicit memory was associated with response enhancements in right IPL. To determine if right IPL correlates of explicit memory for famous faces were associated with familiarity specifically, it was necessary to utilize information from 2 separate contrasts. The general-explicit-memory contrast for famous faces (HEM/LEM,

phase 2) provided neural correlates of explicit memory that were not specific to familiarity. The episodic-familiarity contrast for nonfamous faces (old-know/new, phase 4) provided specific neural correlates of familiarity that were used to identify the familiarity component of the general-explicit-memory contrast for famous faces. Taking into account both of these contrasts, response enhancements in right IPL were attributed to episodic familiarity for famous faces.

Only rarely has it been possible to characterize neural correlates of both conceptual priming and familiarity within the same experiment (Donaldson et al. 2001; Voss and Paller 2006). Nonetheless, many studies have examined these 2 expressions of memory individually. Neuroimaging studies of conceptual priming using verbal materials have frequently associated repeated conceptual processing with response reductions in left anterior IFG (Demb et al. 1995; Buckner et al. 1998; Thompson-Schill et al. 1999; Buckner et al. 2000; Wagner et al. 2000), consonant with both the present conceptual-priming effects in left Brodmann area (BA) 44/45 and with results from studies of short-term semantic priming for words (e.g., Raposo et al. 2006). It is possible that conceptual-priming response reductions in SFG (BA 8) are specific to the current task parameters, as previous conceptual-priming experiments have not uncovered SFG processing. Also, the neural representations operative in conceptual priming may vary with task parameters (cf. Vaidya et al. 1997; Gabrieli et al. 1999).

Whereas recollection is commonly tied to the hippocampus, familiarity has been associated with processing within adjacent rhinal cortex (Aggleton and Brown 2006; Eichenbaum et al. 2007), which could act to facilitate hippocampal pattern classification by, for instance, decorrelating inputs to the hippocampus (Leutgeb et al. 2007). Another possibility is that entorhinal cortex computations are sufficient to support familiarity in isolation (Bussey et al. 2005; Saksida et al. 2006; Danckert et al. Forthcoming). Mounting evidence supports the role of parietal cortex in explicit memory (reviewed in Wagner et al. 2005), and indicates that distinct regions of parietal cortex differentially support recollection and familiarity (Wheeler and Buckner 2004; Yonelinas et al. 2005; Vilberg and Rugg 2007). One popular hypothesis is that parietal cortex interacts with medial temporal structures to coordinate retrieval (Vincent et al. 2006). Yet, the specific mnemonic operations performed by parietal cortex remain unclear. Prior studies using verbal stimuli have frequently associated IPL fMRI activations with recognition memory (reviewed in Wagner et al. 2005). Familiarity as distinct from recollection has been associated with both left IPL (Wheeler and Buckner 2004; Montaldi et al. 2006) and right IPL (Sharot et al. 2004; Wheeler and Buckner 2004; Yonelinas et al. 2005). Two studies have found that IPL activity is directly proportional to familiarity strength in the left hemisphere (Montaldi et al. 2006) and right hemisphere (Yonelinas et al. 2005).

Previous studies of familiarity have employed words or nameable images as stimuli, and IPL laterality has not varied consistently with stimulus category (for instance, picture stimuli familiarity activated left IPL in Montaldi et al. 2006, and right IPL in Yonelinas et al. 2005). In the present study, familiarity-related activity was seen only in the right IPL, perhaps because stimuli were faces rather than words or nameable pictures, thus emphasizing right-hemisphere processing (for instance, right parietal activity has been linked to

the formation of face–name associations; Sperling et al. 2001). The neural correlates of familiarity that we identified are thus consistent with a growing body of literature linking IPL to familiarity. Some studies have also found that recollection elicits greater IPL activity than familiarity in the left hemisphere (Henson et al. 1999; Eldridge et al. 2000; Wheeler and Buckner 2004; Yonelinas et al. 2005) and right hemisphere (Eldridge et al. 2000; Yonelinas et al. 2005), indicating either that IPL is not entirely selective for familiarity or that recollection trials entail higher levels of concomitant familiarity than recognition decisions based only on familiarity.

In summary, our fMRI results are in harmony with previous investigations of conceptual priming and familiarity and collectively indicate that a single memory test can produce neural correlates of both conceptual priming and familiarity—neural correlates that can be teased apart by including behavioral measures of each memory type.

Our results are in keeping with the general distinction made in the fMRI literature between response enhancements associated with explicit memory and response reductions associated with implicit memory. However, familiarity has also been associated with response reductions in entorhinal cortex (Henson et al. 2003), and heightened responses in a variety of brain regions have been associated with implicit memory in several tasks (reviewed in Henson 2003). Instead of relying on the assumption that activity enhancements reflect explicit memory and activity reductions reflect implicit memory, it is thus critical that any neuroimaging investigation include relevant behavioral measures in order to substantiate relationships between memory and corresponding neural measures, as recommended by Paller et al. (2007), and as were included in the present experiment.

We previously used similar procedures to elicit neural correlates of conceptual priming and explicit memory for famous faces with ERP measures (Voss and Paller 2006). Spatiotemporally distinct potentials were identified for these memory phenomena; early-onset potentials maximal over the front of the head were attributed to conceptual priming and late-onset potentials with a posterior distribution were attributed to explicit memory. The present fMRI findings are consistent with this electrophysiological dissociation, although it is essential to note that a given pattern of electrical activity on the scalp could be produced by any of an infinite set of configurations of neural generators (Urbach and Kutas 2002), and so it is currently unclear if previously identified ERP effects map onto their respective fMRI effects reported here. The present fMRI results thus add anatomical specificity that was not provided by our previous scalp-recorded electroencephalography data.

The analyses of ERP correlates of familiarity by Voss and Paller (2006) were based on data collected in an earlier study in which familiarity for nonfamous faces was specifically isolated (Yovel and Paller 2004), and Donaldson et al. (2001) did not behaviorally separate familiarity from other explicit memory processes in their fMRI study. In contrast, the present results included specific measures of familiarity to validate dissociations between fMRI correlates of conceptual priming and familiarity.

In conclusion, neural processing that supports familiarity can be dissociated from neural processing that supports conceptual priming even when both phenomena are elicited by the same set of stimuli during the performance of a single behavioral task (phase 2). This finding indicates that functional dissociations between these 2 memory processes, already identified in amnesic patients, extend to the organization of intact memory systems.

Supplementary Material

Supplementary material can be found at: http://www.cercor. oxford journals.org/

Notes

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