The Functional Neuroanatomy of Episodic and Semantic Autobiographical Remembering: A Prospective Functional MRI Study

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Abstract

■ Autobiographical memory comprises episodic and semantic components mediated by dissociable states of consciousness, one promoting the experience of the self at a specific moment in the past, and the other involving self-knowledge that does not require "mental time travel." These components can be difficult to dissociate using retrospective autobiographical stimuli collection. In this study, we manipulated the episodic/semantic distinction within prospectively collected autobiographical stimuli. Over several months, participants made recordings documenting specific episodes, repeated episodes, and world knowledge. These recordings were later played back to participants during scanning with functional MRI. The results indicated overlapping but distinct patterns of brain activity corresponding to episodic and semantic autobiographical memory. Both episodic and semantic autobiographical memory engaged the left anteromedial prefrontal cortex associated with self-reference, but the episodic condition did so to a greater degree. The episodic condition uniquely engaged the medial temporal, posterior cingulate, and diencephalic regions associated with remote memory recovery. Whereas the episodic condition engaged the right temporo-parietal cortex involved in reconstruction of spatial context and attentional orienting, the semantic condition engaged the left temporo-parietal and parieto-frontal systems involved in egocentric spatial processing and top-down attentional control. Episodic recollection was also associated with suppression of emotional paralimbic regions. These findings support a functional neuroanatomical dissociation between episodic and semantic autobiographical memory, providing concordance to amnesic syndromes with disproportionate impairment in one of these two forms of autobiographical memory. ■

INTRODUCTION

Episodic memory entails the subjective experience of the self at a specific place and time in the past (Tulving, 2002; Wheeler, Stuss, & Tulving, 1997). Evidence for the dissociation of episodic from semantic memory (general knowledge about the world and oneself) is garnered from studies of patients with disproportionate impairment in one of these memory systems (Kapur, 1999). This dissociation is harder to achieve in healthy adults, where both episodic and semantic processes actively support memory performance. Although self-reports obtained with the remember/know technique (Tulving, 1985) can separate the contribution of episodic and semantic processes in the laboratory, such studies sample only a small fraction of the time spectrum involved in human memory using stimuli of questionable personal significance. By comparison, autobiographical recollection is rich in associations and conveys a sense of "the self in subjective time" (Tulving, 2002). Recent functional neuroimaging studies of autobiographical memory have emphasized a left-lateralized fronto-temporo-parietal network, but not exclusively (Conway, Pleydell-Pearce, Whitecross, & Sharpe, 2002; Maguire, 2001). Furthermore, foci within this network are variable across studies.

Studies of autobiographical memory must contend with the lack of experimental control over prior rehearsal, personal significance, emotionality, and retrieval effort inherent in the use of retrospectively sampled personally experienced events. Selection of autobiographical memories in response to cues or interviews reveals characteristics of accessible self-generated autobiographical material, but this material contains a mixture of episodic and semantic memory (Levine, Svoboda, Hay, Winocur, & Moscovitch, 2002; Conway, 2001). Accordingly, Galton (1879), who originated a now-widely used cueing technique (Rubin, 1982), reported that it "shows much less variety in the mental stock of ideas

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than I had expected, and makes us feel that the roadways of our minds are worn into very deep ruts.''

Few neuroimaging studies have attempted to dissociate episodic from semantic aspects of autobiographical memory. Maguire and Frith (2003a), Maguire, Vargha-Khadem, and Mishkin (2001), and Maguire and Mummery (1999) contrasted patterns of brain activation in response to personally relevant sentences generated from an earlier interview and divided into two groups according to their temporal specificity (e.g., ''You were Mike's best man at his wedding'' vs. ''Ray is the youngest of your brothers''). The former was associated with left-lateralized medial frontal, hippocampal, and temporal polar activation. Their 8-sec fact verification task, however, may not have fully evoked the conscious state of autobiographical recollection (Conway, Pleydell-Pearce, Whitecross, & Sharpe, 2002), in which case the findings may under-represent the neural correlates of autobiographical memory.

More vivid episodic recollection of autobiographical events can be evoked by highly specific retrieval cues encountered in everyday life (e.g., revisiting a particular scene) (Conway, Pleydell-Pearce, Whitecross, & Sharpe, 2002). Construction of such cues for research purposes requires advance knowledge of events from the participants' lives. To this end, a few studies have used prospective collection of autobiographical events for later testing (Conway, Collins, Gathercole, & Anderson, 1996; Brewer, 1988; Barclay & Wellman, 1986; Wagenaar, 1986; Linton, 1975). When these events are distinctive, they provide highly specific retrieval cues that promote vivid recollection of everyday episodes (Brewer, 1988), engaging episodic memory and its accompanying state of autonoetic (self-knowing) consciousness (Wheeler et al., 1997). Repeated events, although clearly recognized as autobiographical, are not vividly recollected; they are rather ''known'' or experienced within noetic consciousness (Wheeler et al., 1997).

In the present study, we probed the neural correlates of these two states of consciousness by exposing participants to their own prospectively collected autobiographical and non-autobiographical audiotaped recordings. For 6 to 8 months before the scanning session, participants documented everyday events using a microcassette recorder. They were scanned with functional magnetic resonance imaging (fMRI) while they listened to a random selection of these personal episodic (PE) recordings for the first time. Contamination due to rehearsal or reactivation of the recorded material prior to scanning was minimized by random selection from a large pool of candidate recordings and the absence of exposure to the recordings from the time of their creation to the time of scanning.

There were two conditions of autobiographical recordings: personal episodic (PE; unique events described in detail) and personal semantic (PS; repeated events). The PE recordings provided a high-fidelity representation of participants' original experience and therefore promoted vivid episodic memory during scanning to a greater degree than did the routines and habits described by the PS recordings. Non-autobiographical control conditions included another person's episodes (other episodic; OE) and general semantic knowledge (GS). All conditions comprised recordings dictated by the participant, controlling for auditory–linguistic stimulation.

Hypotheses regarding the pattern of findings in relation to these conditions were based upon evidence from patients with memory impairment and from functional neuroimaging research. Because brain damage can selectively affect autobiographical episodic memory in the face of preserved semantic memory (including PS memory; Conway & Fthenaki, 2000; Kapur, 1999) and because single autobiographical events are dissociated from repeated autobiographical events in functional brain imaging (Maguire & Frith, 2003a; Maguire, Vargha-Khadem, et al., 2001; Maguire & Mummery, 1999), it was hypothesized that the pattern of brain activity evoked by the PE recordings would be dissociated from that evoked by the three nonepisodic memory conditions (PS, OE, and GS), all of which are semantic even though they are superficially dissimilar. This pattern should include medial temporal/diencephalic regions classically associated with memory retrieval as well as left prefrontal and parietal regions (Conway, Pleydell-Pearce, Whitecross, & Sharpe, 2002; Buckner & Wheeler, 2001; Maguire, 2001).

It is also the case that PS and PE memory are both autobiographical. The patterns of activity associated with PE and PS should therefore also have shared elements as well as differences (Maguire & Frith, 2003a; Maguire & Mummery, 1999). For example, recent functional neuroimaging research has indicated left anteromedial prefrontal cortical activation during self-related information processing (Kelley et al., 2002; Gusnard, Akbudak, Shulman, & Raichle, 2001; Craik et al., 1999; Frith & Frith, 1999). Activity in this region should be observed in relation to both PE and PS, as both of these conditions evoke self-reference.

These hypotheses were tested with two analysis methods. The first, partial least squares (PLS; McIntosh, Bookstein, Haxby, & Grady, 1996), is a multivariate method that operates on the covariance between the percentage signal change within voxels and the experimental design to identify a limited number of components (latent variables [LVs]) that optimally relate the two. Each LV represents an experimental effect, and identifies both the pattern of the effect and the voxels showing this pattern. The resulting activation (salience) maps reflect brain networks, with peaks representing nodes in the networks.

There are two main advantages to this approach over standard univariate analysis methods. First, in the standard approach, contrasts among conditions are specified by the experimenter. In PLS, the contrasts among conditions are determined statistically, providing a more conservative test of hypotheses concerning dissociations among conditions. Second, instead of considering each voxel separately, PLS considers the brain as a whole and is thus able to detect brain-wide systems that covary with condition. This approach is well suited to autobiographical memory, a multidimensional cognitive process engaging regions mediating imagery, attention, and emotion in addition to those engaged by basic mnemonic operations.

In the second set of analyses, activity in peak voxels identified by PLS was compared across conditions. These post hoc tests confirmed and extended the PLS results for specific contrasts across conditions at the voxel level, similar to standard univariate analysis methods.

RESULTS

Ratings of Vividness

Analysis of ratings taken in the scanner immediately after each recording indicated that the PE condition was more effective at evoking vivid recollections than the other conditions (see Table 1). The main effect of condition on ratings was significant [$F(3,12) = 49.86, p < .0001$], with significantly higher ratings for PE than for the other conditions (all p's $< .0001$), which did not differ. This pattern held for each rating except for visual imagery, where PE recordings were rated significantly higher than the GS and OE recordings (p's $< .0001$ and .005, respectively), but fell short of significance in comparison to the PS recordings ($p < .06$). PS recordings were rated significantly higher than GS recordings ($p < .01$).

Brain Imaging Data

Two LVs emerged from the task PLS analysis (see Figure 1). The first distinguished PE from the other three conditions, indicating a pattern of brain activity associated with vivid autobiographical episodic recollection. The second distinguished PS from GS; PE and OE did not contribute to the pattern.

Latent Variable 1: PE vs. PS, OE, and GS

As seen in Table 2 and Figure 2, the LV1 pattern included large areas of activation along the frontal and posterior midline cortex, including the bilateral retrosplenial/posterior cingulate cortex extending dorsally to the precuneus, and the bilateral anteromedial prefrontal and dorsal paracingulate cortex. The prefrontal activation was greater in the left hemisphere. Prefrontal cortical activity was also noted in the left ventrolateral region and, to a much lesser degree, in the right mid-dorsolateral region. Bilateral mediodorsal premotor activity was also observed in Brodmann's area (BA) 6. There was a large diencephalic cluster with peaks proximal to the right anterior nucleus and left pulvinar of the thalamus. There was also activity in the right brainstem.

In the temporal lobes, the largest area of activation was in the right temporo-parietal junction, with a smaller cluster in its left analogue. Medial temporal activity was localized to the right parahippocampal gyrus and the left fusiform gyrus. Small cerebellar clusters were also observed.

Regions with negative saliences (i.e., less activity in PE relative to PS, OE, and GS) included the right ventromedial prefrontal cortex, the left superior temporal gyrus, a large left inferior parietal cluster, the left primary motor cortex, and the primary visual cortex.

Latent Variable 2: PS vs. GS

Table 2 and Figure 3 indicate LV2 saliences dissociating PS from GS. As observed for LV1, PS was associated with activity in the left anteromedial prefrontal cortex, the right mid-dorsolateral prefrontal cortex, and the premo-

Table 1. Subjective Ratings across Scanning Conditions[a]

	Thoughts, Emotions		*Visual*		*Overall*		*Episodic Fluency*	
Condition[b]	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
PE	7.9[c]	1.6	8.2[d]	1.5	8.2[c]	1.4	7.8[c]	2.1
PS	2.7	1.1	5.7[e]	2.2	2.6	1.2	2.2	1.2
OE	2.1	1.2	3.7	1.5	2.4	1.1	1.9	1.2
GS	1.8	1.1	2.2	1.1	1.9	1.1	1.6	1.3

[a] Maximum rating = 10.

[b] PE = personal episodic; PS = personal semantic; OE = other episodic; GS = general semantic; Episodic fluency = ease with which an episodic memory came to mind.

[c] Indicates higher ratings in PE relative to all conditions.

[d] Indicates higher ratings in PE relative to GS and OE.

[e] Indicates higher ratings in PS relative to GS.

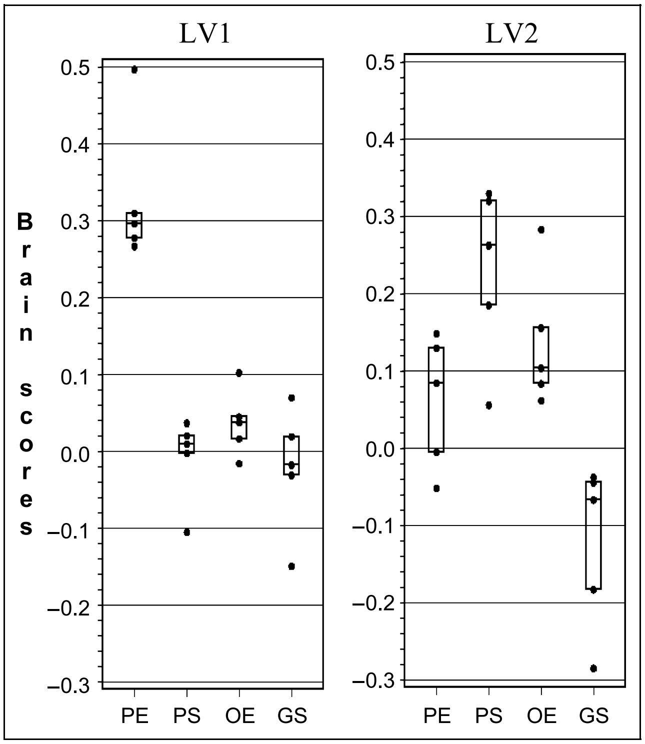

Figure 1. Brain scores associated with LV1 and LV2. Brain scores indicate the degree to which the pattern of activity identified by the LV is expressed by each subject in each condition. Each circle represents one subject. Scores are shown for the four conditions, PE, PS, OE, and GS. The upper and lower lines of boxes represent the 75th and 25th percentiles. The center horizontal line represents the 50th percentile.

tor cortex. The diencephalic cluster had peaks in the right pulvinar and left ventrolateral thalamic nuclei. These clusters were generally smaller than those observed for LV1.

The pattern associated with PS, however, was not merely a lesser version of the PE pattern. Midline posterior cortical activity did not contribute to the LV2 pattern, yet left parietal activity (associated with negative saliences in LV1) was prominent. In addition to premotor BA 6 seen with PE, PS was associated with activity in premotor BA 8. Temporo-parietal junction activity related to PS was greatest on the left, whereas the opposite lateralization was seen in relation to PE. Similarly, parahippocampal activity was noted on the left in PS, whereas this was right-lateralized in PE. Visual cortex deactivation was observed over a larger area than in PE, extending to the dorsal and inferotemporal/occipital visual association cortex.

Supplementary Voxelwise Analyses

Supplementary hypothesis-driven analyses directly compared the effects of PE and PS on signal change in representative regions selected from Table 2 (see Figure 4). For comparison, GS was included in these analyses; OE was omitted for simplicity. The top panel of Figure 4 shows peaks associated with LV1. Signal change in the left anteromedial prefrontal cortex and the left anterior nucleus of the thalamus (c and g in Table 2) was significantly higher in PE than both PS and GS. Signal change in the left ventrolateral prefrontal cortex, the right posterior cingulate cortex, and the left premotor area (e, k, and a in Table 2) was significantly higher for PE than in GS; PS did not differ from GS in these regions. The bottom panel of Figure 4 shows peaks associated with LV2, where signal change associated with PS was similar to or higher than PE. Signal change at the right dorsolateral prefrontal, bilateral temporo-parietal, and right occipital peaks (d and h, and n in Table 2) was similar across PE and PS. PS alone showed greater signal change than GS in the left premotor area 8, the left superior parietal cortex (area 7), and the pulvinar of the right thalamus (b, m, and g, in Table 2). In the left inferior parietal region (top panel; l in Table 2), PS showed greater signal change than PE. These findings confirm distinct but partially overlapping patterns of brain activity associated with listening to PE and PS recordings.

DISCUSSION

This study contrasted patterns of brain activation associated with different forms of autobiographical and nonautobiographical memory evoked by recordings created by participants several months prior to fMRI scanning. In comparison to retrospective techniques for surveying autobiographical memory, this prospective method allowed a high degree of experimental control over stimulus characteristics. It also allowed for the study of everyday autobiographical episodes inaccessible via the

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Notes to Table 2:

[a] Italic indicates negative salience.

[b] Localization (Brodmann's areas) determined with the assistance of the Talairach atlas.

[c] Regional designation for cross-reference to Figures 2, 3, and 4.

[d] Number of voxels in cluster.

[e] Bootstrap ratio, interpreted similar to *z*-score.

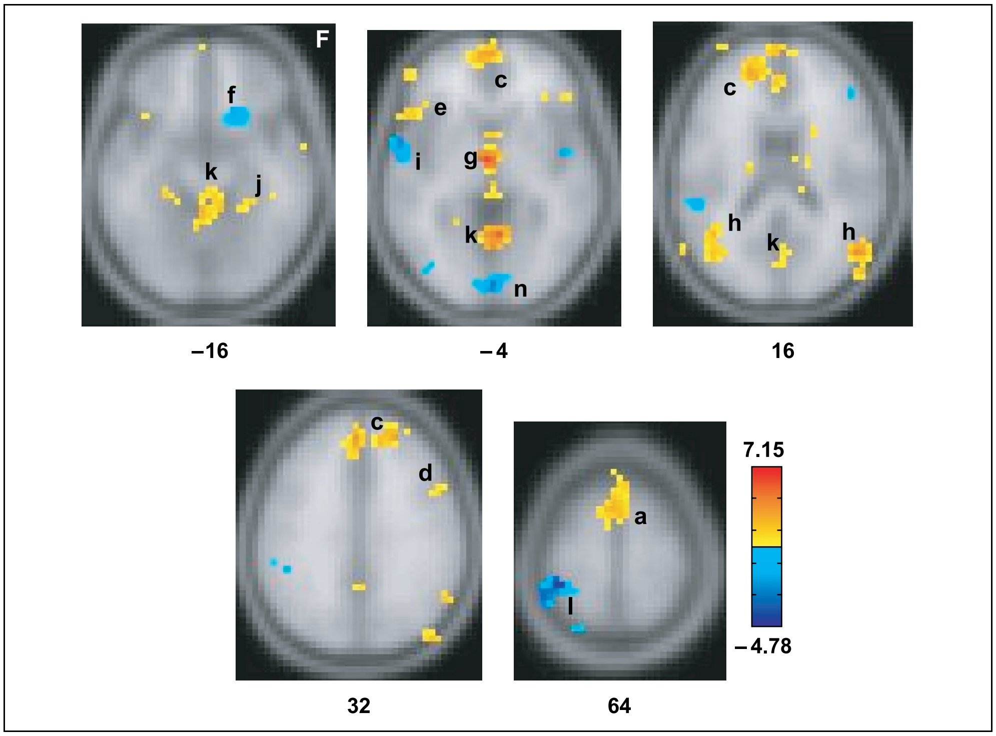
[f] For LV1, number of participants (of 5) showing greater activity in response to PE than in response to PS, GS, and OE (combined). For LV2, number of participants showing greater activity in PS relative to GS.

[g] Coordinates converted from MNI to Talairach space Negative × Coordinates are left hemisphere.

Table 2. Saliences Associated with LV1 (PE vs. PS, GS, and OE) and LV2 (PS vs. GS)[a]

		Latent Variable 1						*Latent Variable 2*					
Region[b]	*Figure*[c]	*Size*[d]	*Ratio*[e]	*No. of Subjects*[f]	*x*[g]	*y*	*z*	*Size*	*Ratio*	*No. of Subjects*	*x*	*y*	*z*
Premotor (6)	a	68	4.37	5	−4	11	58	10	3.78	5	12	11	62
								14	*−4.07*	*5*	*−12*	*−24*	*64*
Premotor (8)	b							12	3.60	5	−28	26	54
								10	4.25	5	−16	33	35
								11	4.48	5	−4	30	46
Anteromedial PFC (9, 10)	c	293	5.54	5	−16	59	19	37	4.86	5	−4	55	19
								20	4.45	5	−12	52	31
Dorsolateral PFC (9)	d	18	4.58	5	48	13	32	18	4.24	4	51	21	25
Ventrolateral PFC (45, 47)	e	61	4.20	5	−55	23	−8						
Ventromedial PFC (111)	f	*25*	*−4.32*	5	*20*	*26*	*−18*						
Precentral (4)		*45*	*−4.30*	*5*	*−16*	*−28*	*71*						
Diencephalic	g	81	7.15	5	4	−4	4	13	4.24	5	−12	−15	4
		54	5.69	5	−4	−27	9	11	3.46	5	12	−34	16
Brainstem		69	4.89	5	4	−36	−25						
Temporo-parietal (39)	h	32	4.22	4	−44	−54	17	105	6.05	5	−51	−68	29
		110	3.90	5	51	−57	29	17	4.48	4	59	−61	29
Lateral temporal (22)	i	*39*	*−4.71*	4	*−59*	*0*	*0*						
		10	*−3.51*	*5*	*−55*	*−34*	*16*	15	4.31	5	59	−50	3
Parahippocampal (35, 36)	j	18	3.16	4	28	−36	−12	11	3.80	5	−28	−28	−25
Inferiror temporal (20, 37)		19	3.81	4	−32	−40	−18						
Posterior cingulate (29, 31)	k	208	7.08	5	4	−50	3						
		39	6.13	5	0	−49	39						
Inferior parietal (40)	l	*125*	*−4.78*	*5*	*−48*	*−40*	*57*	13	3.54	4	−51	−41	39
Superior parietal (7)	m							26	3.97	5	−40	−59	55
Occipital (17, 18, 19)	n	*35*	*−4.47*	*5*	*−4*	*−85*	*4*	*13*	*−4.83*	*5*	*−36*	*−93*	*8*
								145	*−6.85*	*5*	*4*	*−93*	*8*
Cerebellum		12	4.35	5	−8	−87	−29	18	4.17	5	28	−48	−18
								44	4.26	5	8	−56	−41

Figure 2. Singular images showing minima and maxima for LV1 (PE vs. PS, GS, and OE). Numbers below each image correspond to coordinates on the *z* plane in standard space. Color bar indicates degree of activation in standard units (bootstrap ratio).



general retrieval cues used in other studies, yet of considerable importance to personal identity and goal-directed behavior.

We manipulated the episodic/semantic distinction by including conditions involving personal (PS) and nonpersonal (OE, GS) semantic stimuli in addition to the PE stimuli that referenced a specific, verified personal past event relatively uncontaminated by subsequent reactivation. This latter condition was very effective at engaging a feeling of autobiographical recollection, as confirmed by ratings taken at the time of scanning.

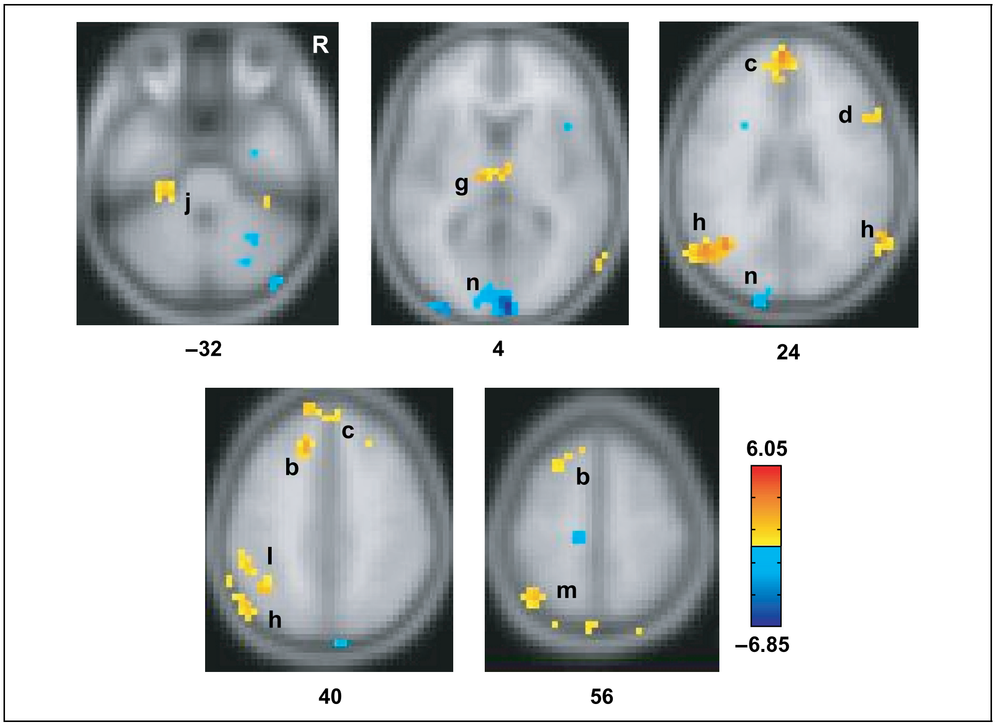
The task PLS results were consistent with our predictions that PE memory would be dissociated from personal and non-PS memory, that PE and PS memory would involve partially overlapping systems, and that, within semantic memory, PS memory would be dissociated from non-PS memory. These results obtained even though the contrasts were not specified a priori, as in standard univariate analysis methods. These patterns can be described in relation to neuroanatomical systems mediating four states of information processing: remote memory recovery, selection, monitoring and self-reference within working memory, attention and spatiomotor imagery, and emotion.

Remote Memory Recovery

PE recordings were specifically associated with activity in functionally linked medial temporal lobe and diencephalic structures classically associated with long-term memory processing. Parahippocampal and related caudomedial cortices are convergence zones for neocortical association areas and are major sources of afferents to the hippocampal complex in the monkey (Suzuki & Amaral, 1994). The hippocampus and midline diencephalic nuclei are richly interconnected and are considered part of a functional system critical to episodic encoding and recall (Papez, 1937). The caudomedial cortices, frequently engaged by autobiographical memory retrieval (Maguire & Frith, 2003a; Piefke, Weiss, Zilles, Markowitsch, & Fink, 2003; Ryan et al., 2001; Maguire, Mummery, & Buchel, 2000; Maguire & Mummery, 1999; Fink et al., 1996), are connected to the hippocampus both directly (Rosene & Van Hoesen, 1977) and indirectly via the anterior thalamus (Vogt & Pandya, 1987), thus mediating hippocampal/midline diencephalic communication.

The enhancement of medial temporal and diencephalic activation in relation to hearing PE recordings corresponds to the richness of recovered episodic information reflected in subjects' behavioral ratings. PS, which evoked generalized rather than specific past events, was associated with activity in the ventrolateral and pulvinar nuclei connected to the lateral temporal and parietal cortex (Yeterian & Pandya, 1985, 1991), but not with the anterior nuclei connected with the hippocampus. This dissociation was confirmed in the post hoc voxelwise analyses, where the largest difference in activity evoked by PE and PS was observed at the anterior thalamic peak, whereas right pulvinar activity was more specifically associated with PS. Whereas parahippocampal activation in response to PE was primarily right-sided, PS was associated with activity in the left parahippocampal gyrus. The parahippocampal gy-

Figure 3. Singular images showing minima and maxima for LV2 (PS vs. GS). Numbers below each image correspond to coordinates on the *z* plane in standard space. Color bar indicates degree of activation in standard units (bootstrap ratio).



rus, although clearly involved in episodic retrieval, also supports semantic operations and familiarity (Brown & Aggleton, 2001; Vargha-Khadem et al., 1997). Our data suggest the parahippocampal contribution to semantic autobiographical retrieval may be left-lateralized for the class of PS stimuli used in this study (see also Maguire & Frith, 2003a; Maguire & Mummery, 1999).

Although the hippocampus was implicated via activation of connected structures, we did not observe activation within the hippocampus itself. Hippocampal activation has been found in some (Maguire & Frith, 2003a; Piefke et al., 2003; Ryan et al., 2001; Maguire, Mummery, et al., 2000; Maguire & Mummery, 1999), but not all functional neuroimaging studies of autobiographical memory (Nyberg, Forkstam, Petersson, Cabeza, & Ingvar, 2002; Conway, Turk, et al., 1999). It is possible that our image acquisition parameters were insensitive to changes in hippocampal activity without greater statistical power, or that the hippocampus was not differentially activated in relation to the control conditions. We also speculate that the highly specific retrieval cues in the PE recordings may have automatically bound and coactivated nodal cortical sites involved in mnemonic re-representation, a function that would have been mediated by the hippocampus had the external retrieval cues been less specific.

Selection, Monitoring, and Self-Reference within Working Memory

Prefrontal cortical activations are likely a consequence of mnemonic control operations related to processing the autobiographical narrative stream. In keeping with most previous studies of autobiographical memory retrieval (Conway, Pleydell-Pearce, Whitecross, & Sharpe, 2002; Maguire, 2001), prefrontal activation in this study was strongly biased to the left. Left ventrolateral prefrontal activation was strongly and specifically related to PE recordings, indicating maintenance and selection demands within working memory (Fletcher & Henson, 2001), perhaps related to enhanced elaboration and self-cueing for retrieval evoked by the PE narratives (Buckner & Wheeler, 2001). The left anteromedial prefrontal and paracingulate regions are frequently engaged by autobiographical stimuli (Conway, Pleydell-Pearce, Whitecross, & Sharpe, 2003; Maguire & Frith, 2003a; Nyberg et al., 2002; Conway, Pleydell-Pearce, & Whitecross, 2001; Ryan et al., 2001; Conway, Turk, et al., 1999; Maguire & Mummery, 1999). More generally, they are associated with self-referential information processing (Kelley et al., 2002; Gusnard et al., 2001; Craik et al., 1999; Frith & Frith, 1999). Consistent with the literature on self-reference, we found activity in these regions in relation to personal (PE and PS) but not impersonal (OE and GS) material. Based on the connectivity of these regions with medial temporal and diencephalic regions via the cingulum bundle (Morris, Petrides, & Pandya, 1999), one might predict greater activity in relation to the episodic stimuli. Accordingly, our data suggest greater engagement by stimuli invoking the episodic "self in subjective time" (Tulving, 2002) relative to the comparatively timeless self-characterized by PS, as confirmed by a significant PE–PS difference in the direct voxelwise comparison at this peak.

Right mid-dorsolateral regions are involved in monitoring and manipulation of retrieval products (Fletcher & Henson, 2001), especially in later phases of retrieval (Duzel et al., 2001). Both autobiographical memory conditions (PE and PS) were associated with activity in these regions, possibly reflecting sustained autobiographical processing, although the sizes of these clusters were relatively small. Right mid-dorsolateral activity is infrequently reported in other studies of autobiographical memory, possibly due to the use of briefer stimuli or control tasks that engaged similar working memory operations (for exception, see Conway, Pleydell-Pearce, & Whitecross, 2001).

Attention and Spatiomotor Imagery

Visuospatial processing, including the inspection of imageable representations and retrieval of spatial context important to recollection of specific autobiographical events (Conway & Pleydell-Pearce, 2000), is mediated by the medial temporal and parietal regions engaged by PE (Burgess, Maguire, Spiers, & O'Keefe, 2001). The polymodal association cortex at the temporo-parietal junction, activated in association with PE and PS, has been implicated in the interpretation of others' movements, goals, and intentions (Frith & Frith, 1999). The engagement of these regions in studies of autobiographical memory (Maguire & Frith, 2003b; Nyberg et al., 2002; Ryan et al., 2001; Conway, Turk, et al., 1999; Maguire & Mummery, 1999) might therefore be attributed to mental imagery of past movements and behaviors.

Maguire and colleagues reported temporo-parietal junction activation in association with PE and PS stimuli (Maguire & Frith, 2003a; Maguire & Mummery, 1999). This activation was bilateral in a PET study (Maguire & Mummery, 1999), but left-lateralized in an fMRI study (Maguire & Frith, 2003a). Our data suggest dissociations among right and left temporo-parietal foci. Consistent with lateralization of activation in the parahippocampal gyrus, temporo-parietal activation in relation to PE was much more extensive in the right hemisphere than in the left. Similar activity in a study of EEG slow cortical potentials was attributed to sensory–perceptual processing occurring in later epochs following autobio-

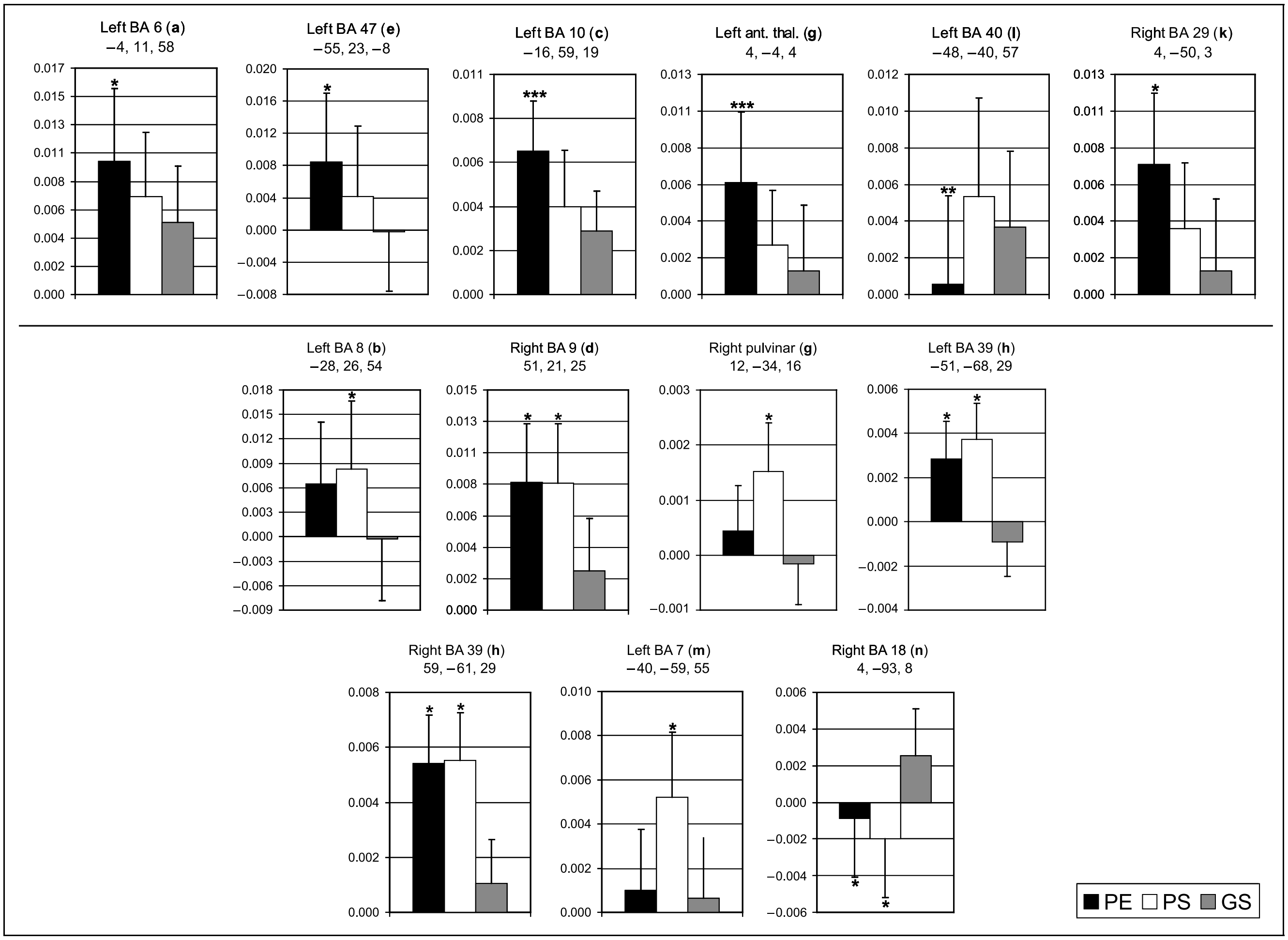


Figure 4. Plots of signal change from baseline for PE, PS, and GS at selected LV1 (top) and LV2 (bottom) peaks. Letters and coordinates correspond to peaks specified in Table 2. * = significantly different from GS; ** = significantly different from PS; *** = significantly different from PS and GS.

graphical memory formation (Conway, Pleydell-Pearce, & Whitecross, 2001).

Temporo-parietal activation in relation to PS was much larger in the left hemisphere and localized superiorly relative to PE (accounting for the left parietal negative saliences in LV1). The left parietal regions engaged by PS are involved in manipulating visuospatial representations of body schema (Gerstmann, 1957). Accordingly, most of the PS stimuli reported repeated acts from an egocentric perspective requiring minimal reconstruction of spatial context. The unique PE events used here, on the other hand, were more reliant on the reconstruction of spatial context mediated by the right medial temporal, medial parietal, and temporo-parietal regions (Burgess, Becker, King, & O'Keefe, 2001).

Both PE and PS were associated with activity in the premotor cortex, but there were dissociations across these conditions. As observed in other studies of autobiographical memory (Piefke et al., 2003; Nyberg et al., 2002; Ryan et al., 2001; Conway, Turk, et al., 1999) and more generally in studies of retrieval from short- and long-term memory (Cabeza & Nyberg, 2000), both PE and PS were associated with activity in the dorsomedial BA 6 bilaterally, which is reciprocally connected to the anteromedial area 9 (Barbas, Ghashghaei, Dombrowski, & Rempel-Clower, 1999). PS, however, was associated with additional increased signal in the left dorsal BA 8, which receives projections from the left parietal regions also associated with PS (Petrides & Pandya, 1984), possibly related to direction of gaze in personal space.

The patterns of parietal, temporo-parietal, and frontal activity engaged by PE and PS can be interpreted within a dual attentional systems framework in which a bilateral dorsal frontoparietal system is involved in top-down stimulus and response selection and a right-lateralized temporo-parietal/ventral frontal system is involved in sensory orienting towards more novel behavioral relevant stimuli (Corbetta & Shulman, 2002). The former system (in this case, greater in the left hemisphere) was engaged by recognition of repeated, internally driven acts comprising the PS stimuli, whereas the latter was engaged by recognition of the PE stimuli that carry relatively novel information concerning social and physical relations in one's environment.

PE and PS were associated with deactivation of the primary and association visual cortex. This finding may relate to higher processing of the visual fixation stimulus in OE and GS, which were less engaging of mental imagery than PE and PS. A similar interpretation may apply to the primary motor and auditory association cortex deactivation associated with PE.

Emotion

Other functional neuroimaging studies of self-generated autobiographical material show activations in ventral limbic and paralimbic regions associated with emotion (Markowitsch, Vandekerckhovel, Lanfermann, & Russ, 2003; Piefke et al., 2003; Fink et al., 1996), even when emotional memories are not explicitly requested (Andreasen et al., 1999; Maguire & Mummery, 1999). Recollection of examiner-selected everyday events as done here minimizes emotional content, evoking activation in a dorsal trend reflecting cognitive and sensory processing (Pandya & Yeterian, 1996). Moreover, deactivation of ventromedial prefrontal regions was consistent with dorsal inhibition of ventral paralimbic regions during processing of relatively nonemotional autobiographical episodes (Gusnard et al., 2001; Mayberg, 1997).

Conclusions: Two Forms of Autobiographical Memory

Our results provide functional neuroanatomical evidence for the dissociation of PE and PS autobiographical memory and concordance to amnesic syndromes in which these two forms of autobiographical memory are dissociated (Conway & Fthenaki, 2000; Kapur, 1999). Although it is often assumed that reference to autobiographical events specific in time and place invokes more episodic than semantic processing, this is not always the case (Conway, Pleydell-Pearce, & Whitecross, 2001; Cermak & O'Connor, 1983). Autobiographical stimuli such as those used in many functional neuroimaging studies also invoke semantic constructs such as autobiographical facts, extended events, and lifetime periods (Conway & Pleydell-Pearce, 2000). By randomly selecting from prospectively recorded, unrehearsed, unique events, we optimized stimuli for the obligatory engagement of episodic autobiographical memory, maximizing the contrast to semantic autobiographical memory, operationalized here as repeated events or habits.

In relation to episodic autobiographical memory, the neural correlates of semantic autobiographical memory were indistinguishable from GS and OE, supporting the notion that PS memory can be subsumed under the general construct of semantic memory (Kapur, 1999; Wheeler et al., 1997). Yet there are subcategories within the domain of semantic memory. Our data suggest that PS memory can be dissociated from generic semantic processing (GS) in that it engaged regions involved in self-reference, spatiomotor imagery, and attentional control.

Episodic autobiographical memory entails the integration of self-knowledge with event memory, giving rise to a conscious state of self in subjective time definitive of episodic recollection (Tulving, 2002; Wheeler et al., 1997). Episodic autobiographical recollection engaged the left anteromedial prefrontal regions involved in self-reference to a greater degree than did semantic autobiographical memory, which is often used in studies of self-reference (e.g., Kelley et al., 2002). This region, coactivated with medial temporal lobe and diencephalic regions involved in remote memory recovery, prefrontal regions involved in working memory, and parietal and temporo-parietal regions involved in spatial imagery, allows humans to transcend the mere recognition of past events, to relate them to other events, past and planned, and to use that information to guide future behavior and function effectively as a member of society (Stuss & Levine, 2002; Tulving, 2002; Conway & Pleydell-Pearce, 2000; Frith & Frith, 1999).

METHODS

Collection of Autobiographical Stimuli

Five healthy adults (2 men) aged 26–37 dictated the stimuli into a microcassette recorder. There were four recording conditions, PE, PS, OE, and GS. PE recordings comprised a detailed description of a unique event of no more than a few hours in duration (e.g., helping someone move house), including the story line, sensory information, thoughts, and feelings. Semantic information concerning repeated events was minimized. The average time elapsed from the end of the event to the time of recording was 100 min (*SD* = 62 min).

PS recordings described personal factual information, mostly consisting of repeated activities (e.g., making coffee). OE recordings were created by reading other participants' transcribed PE recordings. The GS condition included readings from a book about the history of Toronto, Canada. In making non-PE recordings, participants avoided information that would trigger PE memories (e.g., ethnic groups in the GS readings associated with a unique personal episode). All recordings were matched for time elapsed from time of recording to scanning. The mean age of recordings across participants was 156 days (range: 151–163; approximately 5 months). Transcribed examples are provided in the Appendix.

A main goal of this study was to create a pool of memories relatively uncontaminated by rehearsal or reactivation prior to scanning. This was accomplished by oversampling to reduce the novelty of the recording activity. The mean number of recordings per participant across all four conditions was 180 (range: 82–424). Of these, 32 (24%) were selected for scanning. For the PE recordings alone, an average of 13% of the total available per subject were selected. Participants were instructed not to listen to any recordings after making them.

Although rehearsal or reactivation could not be completely ruled out, these were reported as minimal by the participants and decreased with increasing time and accumulation of recordings. In rare instances where mental rehearsal occurred, the richness of detail was incomparable to that evoked by listening to the recording. Although the act of recording may have changed the nature of the memory representation, previous research has shown this has little effect, at least as measured by behavioral tests (Thompson, 1982).

Participants were given extensive training on the recording methodology along with a detailed instruction manual and feedback based on their initial recordings. A précis of the instructions was attached to the recorder.

Recordings were edited to 30 sec in length and randomized across four presentation series, each containing two recordings per condition as well as one randomly interspersed rest period of visual fixation, also lasting 30 sec.

fMRI

A 1.5-T MRI scanner (Signa, CV/i hardware, LX8.3 software; General Electric Medical Systems, Waukesha, WI) with a standard quadrature birdcage transmit/receive head coil was used for all experiments. A three-dimensional fast spoiled gradient-echo pulse sequence (TR = 12.4 msec, TE = 5.4 msec, flip angle 35°, 22 × 16.5 cm FOV, 256 × 192 acquisition matrix, 124 axial slices 1.4 mm thick) was used to acquire a T1-weighted volumetric anatomical MRI for each participant. Functional imaging was performed to measure brain activation by means of blood oxygenation level-dependent (BOLD) effect (Ogawa et al., 1992) with optimal signal contrast. Twenty-four axial slices 5 mm thick were obtained using a single-shot T2*-weighted pulse sequence with spiral readout, and off-line gridding and reconstruction (Glover & Lai, 1998) (TR = 2000 msec, TE = 40 msec, flip angle 80°, 90 × 90 effective acquisition matrix, 20 cm FOV). To allow magnetization to reach equilibrium, stimulus presentation was delayed by 20 sec after the onset of repetitive fMRI scanning.

Auditory stimuli were presented using fMRI-compatible headphones (Silent Scan, Avotec, Jenson Beach, FL). During all conditions, participants listened (or rested) while visually fixating on a cross presented centrally on a back-projection screen using an LCD projector (Model 6000, Boxlight, Poulsbo, WA) and viewed through angled mirrors mounted on the head coil. Rating scales (described below) were viewed similarly. Responses were collected with fMRI-compatible key pads (Lightwave Technologies, Surrey, BC, Canada) and custom-designed interactive software.

Immediately after hearing each recording in the scanner, participants had 60 sec to rate vividness on four 10-point scales: imagery, re-experiencing of thoughts and emotions, overall re-experiencing, and how easily the episode came to mind. This was followed by a 10 sec timeout period that contained a verbal cue indicating the next condition and a tone 2 sec before onset of the next recording. Image data from this 70 sec intertrial interval were not analyzed.

Image Analysis

Images were preprocessed using the Analysis of Functional Neuroimages (AFNI) (Cox, 1996) and Statistical

Parametric Mapping (SPM99) software (Wellcome Department of Cognitive Neurology, London, UK). Initial coregistration was performed using AFNI (Cox & Jesmanowicz, 1999) to reduce the confounding effect of head motion on fMRI data quality (the range of head motion was less than 1.5 mm for all subjects). Subsequently, using SPM99, images were spatially transformed to standard space (Evans et al., 1992) using a linear transformation only with sinc interpolation. The resulting voxel size was 4 × 4 × 4 mm. The data were then smoothed spatially with an 8-mm full-width half-maximum gaussian filter. The effect of any global differences in fMRI signal intensity between individual subjects was removed by calculating the percentage signal change for each voxel during the active conditions as compared to the signal intensity during visual fixation for each subject within each run.

The preprocessed fMRI data were then analyzed using PLS (McIntosh et al., 1996; see Introduction). PLS LVs indicate optimal relations between the task design and patterns of activity across the whole brain. Each LV represents an experimental effect, and identifies both the pattern of the effect and the voxels showing this pattern. No statistical correction for multiple comparisons at the voxel level is necessary. Rather, statistical assessment (described below) is done at the image level.

Saliences (i.e., weights) are calculated for each voxel and indicate how much that voxel contributes to a particular LV. A salience can be positive or negative, depending on the voxel's relation to the pattern identified by the LV. Voxelwise multiplication of the salience with the signal change and summing over all voxels gives a ''brain score'' for each subject on a given LV that indicates the degree to which the pattern of activity identified by the LV is expressed in each subject in each condition. Plotting these scores across conditions shows how patterns of brain activity associated with a particular LV are related to the experimental design (see Figure 1).

Most of the earlier behavioral work using this prospective method of collection of autobiographical events involved one or very few subjects (usually the experimenter, e.g., Linton, 1975). Because of the sample size, several steps were taken to ensure the reliability of the findings, including the use of permutation tests, a high spatial extent threshold for reported activations, and single-subject analyses at each peak (see below). Perhaps most importantly, the reliability of the data is supported by their concordance with prior lesion and functional neuroimaging studies. The reliability of brain activation data in spite of the low *n* supports the robustness the retrieval cues contained in the recordings.

The statistical significance of the LVs was assessed using a permutation test, which was repeated 500 times (Edgington, 1980). In this procedure, the scans are randomly reordered to calculate the probability of each LV having occurred by chance. Each repetition within a certain condition was included in the analysis to increase statistical power (i.e., eight observations per condition per subject). The resampling algorithm maintained the repeated-measures nature of the data, ensuring that the exchangeability criterion for permutation tests was satisfied. To determine the reliability of the saliences for the brain voxels characterizing each pattern, the saliences were submitted to a bootstrap estimation of the standard errors (100 samples; Efron & Tibshirani, 1986). The bootstrap procedure helps to reduce the impact of outlier observations.

Voxel clusters were considered significant if they contained at least 10 voxels (i.e., 640 μL) exceeding a bootstrap ratio (salience/standard error, roughly equivalent to *Z* scores) ≥ 3.15 on a given LV. The reliability of these peaks was further assessed by examining the pattern of activation (expressed as percent signal change from the visual fixation baseline) at each peak within each of the five participants. As seen in Table 2, the pattern derived from the group data was consistent for four or five of the five participants. The coordinates of clusters were determined by the location corresponding to the peak bootstrap ratio. Localization was accomplished with the assistance of the atlas by Talairach and Tournoux (1988) following conversion of coordinates to Talairach space using a publicly available conversion program (www.mrc-cbu.cam.ac.uk/Imaging/mnispace.html).

The task PLS analysis did not yield a specific PE versus PS contrast; LV1 contrasted PE to all other conditions, and LV2 contrasted PS to GS. We therefore conducted supplementary hypothesis-driven analyses to examine the relative effect of PE, PS, and GS recordings on signal change from visual fixation baseline at peak voxels selected from Table 2 (see Figure 4), with follow-up comparisons adjusted for multiple comparisons with the Tukey–Kramer method.

The effect of condition on behavioral ratings of vividness was also assessed via ANOVA with follow-up comparisons adjusted for multiple comparisons with the Tukey–Kramer method.

APPENDIX: EXAMPLES OF STIMULI

Personal/Other Episodic

It was the last night of our Salsa dance class lessons. The instructor and several people from our class went out after the class to the Chiquita Night Club on Verana Street. People were dancing all different styles of Salsa. It was quite amazing. There was one fellow who came in quite a bit later and started dancing with the tall dark woman who was wearing all white. He was spinning her around like a top. Then he actually flipped her over his arm at one point and then they continued dancing. Another woman came along and joined them and he was spinning both of them around.

Personal Semantic

I fill the kettle on the stove with cold water or half way up or however many people are having tea. I put that on the stove and light it. I take the teapot with the broken lid and rinse that out with warm water and then I put enough tea bags in it, which are just above the stove. I take those out and I put enough for the people having tea. Then I finish doing whatever I was doing at the time, wait for the kettle to whistle. When the kettle whistles I take the lid off the kettle pour it into the teapot, put the lid back on the teapot.

General Semantic

By 1947, there were 5000 Japanese Canadians living in Toronto. The arrival of a Japanese minister, under the sponsorship of the United Church, marked the beginning of the Japanese Church in Toronto. Early organizations included the Nisi Men and Women's committee, established to help the housing and jobs, the Japanese Canadian Committee for Democracy and the National Japanese Canadian Citizens Association. In the 1950's and 60's, more Japanese Canadians arrived from the West, settling in cities and later moving to the suburbs.

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The data reported in this experiment have been deposited in the fMRI Data Center (http://www.fmridc.org). The accession number is 2-2004-116HX.

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