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Same as it ever was: Vividness modulates the similarities and differences between the neural networks that support retrieving remote and recent autobiographical memories

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ABSTRACT

The comparison of recent and remote autobiographical memories is often confounded by qualitative disparities across memories of different ages, such as vividness. In this study, ten individuals prospectively collected audio recordings that were used to cue memories of recent (~1 month old) and remote (~1.5 year old) everyday events. Because the retrieval cues were recorded at the time of event, they were highly potent. Although remote events did not differ in novelty, importance, or emotional change at the time at the time of encoding, half of the cues for these events induced retrieval comparable in vividness to recent events (all of which were vividly re-experienced). Recent and remote vivid memories were associated with a neural pattern that included right frontal, left parietal and limbic regions that were active early in the retrieval period. Non-vivid remote memories were associated with a later onset of a bilateral distributed pattern that included regions in the frontal, parietal, and temporal lobes. Functional connectivity analysis indicated that the left anterior hippocampus was co-activated with bilateral frontal, parahippocampal, and parietal regions for vivid memories (irrespective of memory age) early in the retrieval period, whereas non-vivid memories, alongside recent memories, showed later and broader co-activation with frontal, parietal, occipital, and temporal regions. The absence of a significant difference between the recent and remote vivid memories may be due to insufficient power to detect potential subtle differences between these conditions. Nonetheless, there was evidence for different patterns of hippocampal–neocortical connectivity for remote memories and recent memories, irrespective of vividness. These findings suggest that while there is a functional shift in hippocampal connectivity that is associated with memory age when very recent events are used, vividness is strongly associated with both activation and functional connectivity patterns irrespective of memory age.

Introduction

Autobiographical memory is a complex capacity that entails recalling factual information, general knowledge about oneself (i.e., personal semantics), and specific episodic elements of an event (Conway, 2001). The latter of these forms the basis of the recollective or autonoetic aspect of autobiographical memory retrieval (Tulving, 2002). This recollective aspect of autobiographical memory is supported by a network of brain regions that includes the medial temporal lobes (MTL), midline prefrontal regions, lateral temporal cortex, and posterior parietal midline regions, with the hippocampus necessary for binding together the multimodal representations of an episode (Addis et al., 2004; Greenberg et al., 2005; Svoboda et al., 2006; Wheeler and Buckner, 2004).

Early models of memory (e.g., the Standard Model of Consolidation; Squire and Alvarez, 1995; Squire and Zola, 1997) indicated that hippocampal–neocortical connections weaken over time as storage of the memory is transferred from the hippocampus to cortical regions (Bayley et al., 2003; Niki and Luo, 2002; Piefke et al., 2003). Challenges to this theory from focal lesion cases (Noulhiane et al., 2007; Rosenbaum et al., 2008; Steinvorth et al., 2005), neuroimaging studies (Gilboa et al., 2004; Piolino et al., 2004; Ryan et al., 2001; Söderlund et al., 2012; Viard et al., 2007), and animal models (Lehmann et al., 2007) support an alternative account: the Multiple Trace Theory (Moscovitch et al., 2005; Nadel and Moscovitch, 1997), which holds that the hippocampus is always engaged by the episodic elements of autobiographical memory, regardless of memory age (For expections, see Bayley et al., 2005, 2006; Kirwan et al., 2008).

The purpose of the present study was to address two relatively unexplored elements of the functional neuroanatomy of recent and remote autobiographical memory retrieval. First, we sought to bring control over qualitative aspects of the retrieved memories that are often confounded with memory age by using highly potent, prospectively collected autobiographical cues. Second, having attained this level of control, we assessed not just the level of hippocampal activation in recent

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versus remote memories, but also similarities and differences in hippocampal connectivity and the neural context accompanying them.

The recency effect is a fundamental principle of memory function that also applies to autobiographical memory (Galton, 1879; Rubin, 1986). Forgetting accelerates exponentially with time, with the greatest amount of forgetting occurring in the days and weeks following an event (Rubin and Schulkind, 1997a,b). In most functional neuroimaging studies of autobiographical memory, remote events that are accessible from cueing are more likely to be well-rehearsed or repeated (e.g., high school graduation) and therefore more schematic, semantic-like, and less vivid, likely entailing less hippocampal engagement (Nadel et al., 2007). They are also likely to fall well outside a crucial period of consolidation or transformation that is estimated to be on the order of weeks or months, based on extrapolation from animal research (Anagnostaras et al., 1999; Bontempi et al., 1999; Remondes and Schuman, 2004; Winocur et al., 2005). In contrast, recent events have not been repeatedly reactivated and are more "vividly" recollected, entailing more hippocampal involvement. In fact, fMRI studies have noted that differences in hippocampal activation between recent and remote memories can be accounted for by differences in vividness (Gilboa, 2004; Kensinger et al., 2011; Rabin et al., 2010). Extending from regional differences, investigations have also reported that the hippocampus shows differential connectivity with other regions of the autobiographical memory network (particularly those associated with visual processing) according to vividness (Daselaar et al., 2008) and memory age (Söderlund et al., 2012).

In order to attain recent and remote memories matched for vividness, we asked participants to prospectively collect retrieval cues for everyday episodes via audio recordings made within minutes or hours of an event's occurrence (Levine et al., 2004, 2009; Svoboda and Levine, 2009) over the course of a two year period. This method allowed us to select precisely dated events from within a time window that cannot be readily sampled by retrospective methods. These cues were inherently unbiased to the mode of retrieval as the later rehearsal or future significance of events (which were all unique, but not of high emotional significance) was unknown at the time the cue is created. At the time of retrieval, events were classified according to their degree of vividness independently from memory age. Because the recordings provided highly potent retrieval cues, they elicited sufficient remote memories matched to recent memories for vividness, allowing us to test hypotheses concerning vividness independently of memory remoteness.

We analyzed brain networks engaged by these retrieval cues for both activation and connectivity. Based on the Multiple Trace Theory (Moscovitch et al., 2006; Nadel et al., 2000) and the notion that vividness modulates hippocampal activity in autobiographical retrieval, we predicted that the hippocampus would be similarly activated for recent and remote autobiographical memories that were matched for vividness. More importantly, we predicted that recent and remote memories matched for vividness would engage a similar pattern of hippocampal–neocortical connectivity distinct from that associated with less vivid remote memories. Based on the hypothesis that vivid memories are more likely retrieved directly (and quickly) via imagery-guided processes whereas non-vivid memories require more effort and time to reconstruct the recalled event (Conway, 2001; Conway and Bekerian, 1987; Greenberg and Rubin, 2003), we also predicted that a hippocampally-dependent vivid autobiographical memory network would peak at earlier time points for directly retrieved vivid memories compared to non-vivid memories.

Materials and methods

Participants

The participants were 10 healthy adults (range = 28 to 41 years old; 5 female). All were free from significant physical or mental illnesses. All participants gave informed consent in accordance with the Rotman Research Institute/Baycrest Hospital ethical guidelines and received compensation for their participation.

Collection of autobiographical stimuli

Participants dictated autobiographical events into a digital recorder as per the methods describe in a previous report (Levine et al., 2004). Event recording occurred one to two years prior to scanning with a mean range of these remote memories being 0.95 to 2.89 years and again at a recent time frame with a mean range of 30 to 95 days prior to scanning. Specifically, participants recorded a detailed description of a unique event (with spatial, sensory, perceptual, thought, and emotion details, as appropriate) that took place over no more than a few hours right after the event took place. The duration of each recording was approximately 60 s, but was allowed to vary as necessary. At the time of the recording, participants also assigned a title to each event and rated the novelty, importance, and emotional change experienced for the event on 0–4 point scales. Highly emotional or personally significant events were excluded from the experiment. Participants were asked not to listen to the recordings after making them.

Autobiographical stimuli

The median number of recordings per participant was 63 with a range of 35 to 244. Depending on the size of the available pool of memories, the number of recent and remote memories selected for scanning was 16 and 32 (5 participants); 15 and 24 (2 participants) or 12 and 20 (3 participants). The mean age of the remote (old) memories across all participants was 565 days (SD = 165) and the mean age of the recent (new) memories was 31 days (SD = 21). All recordings were trimmed to 30 s in length for presentation in the scanner.

Baseline conditions

As a sensorimotor control condition, recordings of reversed speech were created from the participants' own recordings played backwards. Two trials per run were included for a total of eight 30 s trials (with two participants receiving six trials). Seven participants also completed an odd number detection task (Stark and Squire, 2001) during which a series of single-digit numbers was presented one at a time, for 1900 ms with a 100 ms interstimulus interval for 30 s epoch. Participants silently noted whether the number was odd or even. As this condition was not available for all 10 participants, it was not included in this analysis.

Scanner protocol

In the scanner, participants either heard their recordings or performed/heard the baseline task. For the autobiographical recording condition, each event began with an alerting beep, followed 4–5 s later by the title provided by participants at the time of recording (e.g., *having dinner in Kensington Market*) presented on the screen and through headphones. Then the autobiographical recording associated with the cue was played to the participant as they viewed a fixation cross on the center of a computer screen (30 s). After listening to the recording, participants rated the vividness (how much re-experiencing) of the event on a scale of 1 to 10 using an fMRI-compatible response pad, followed by rest until the next event beep-title-recording was presented. For seven of the participants, the duration of this rating/rest period was 20 s. Three of the participants provided additional ratings (thoughts, visual detail and ease of retrieval). For these participants, the rating/rest period was 70 s. As only the vividness rating was available for all participants, the other ratings were not analyzed. Remote (old) were split into high and low vividness (high-old and low-old, respectively) conditions based on each participant's median rating. Participants made the same ratings for all conditions (autobiographical and baseline) in order to confirm that autobiographical

recollection in the memory conditions exceeded that of the baseline conditions.

The autobiographical and baseline trials were randomized across three or four runs (depending on the number of available memories; 4 runs for 7 participants, 3 runs for 3 participants, containing 510 or 550 volumes per run) such that each run contained the same number of each trial type.

Data acquisition

MRI images were acquired with a 1.5 T scanner (Signa, CV/i hardware, LX8.3 software; General Electric Medical Systems, Waukesha, WI). A three-dimensional fast spoiled gradient echo pulse sequence (TR = 12.4 ms, TE = 5.4 ms, flip angle 35°, 22 cm × 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. Functional scans were obtained using a single shot T2*-weighted pulse sequence with spiral readout, achieving 24 slices 5 mm thick (TR = 2000 ms, TE = 40 ms, flip angle 80°, 90 × 90 effective acquisition matrix, 20 cm FOV).

Data processing

All of the images were reconstructed and pre-processed using AFNI (Cox, 1996). To minimize through-slice signal loss and correct for poor image quality in orbitofrontal and medial prefrontal regions due to static field inhomogeneity effects, we employed a z-shim acquisition during fMRI, followed by a combination of z-shimmed images after acquisition with all of our participants (Constable and Spencer, 1999; for a more complex example; Du et al., 2007). During a scan, a given slice was acquired with two different levels of slice selected gradient refocusing amplitude (linear magnetic field shim setting). Combining these scans by using the square root of the sum of squares resulted in higher quality images at the expense of increasing the TR from 2000 ms to 4000 ms. This step was justified given that we were examining a long retrieval period. The data were then motion corrected, transformed into voxels of 4 × 4 × 4 mm, normalized to the Montreal Neurological Institute (MNI) EPI template, and smoothed with an 8-mm isotropic Gaussian filter.

Functional data analysis

The functional data analyses were done with Partial Least Squares (PLS: McIntosh and Lobaugh, 2004; McIntosh et al., 1996; Krishnan et al., 2011). PLS is a flexible multivariate technique that describes the relations between any set of exogenous measures (e.g., experimental design or behavioral measures) and a set of dependent measures (e.g., brain imaging data). PLS is similar to other data-driven multivariate techniques, such as principal component analysis, in that contrasts across conditions are not specified in advance. PLS begins with a covariance matrix between the experimental conditions (i.e., contrasts of memory age and vividness; see results) and each voxel's signal at each lag (TR). The covariance matrix is then decomposed using singular value decomposition (SVD) to produce orthogonal latent variables (LVs) that optimally represent relations between brain voxels and the design (McIntosh and Lobaugh, 2004; McIntosh et al., 1996). The LVs are extracted in order of the amount of covariance explained. Each LV has a singular value that indicates the amount of covariance accounted for by the LV. The significance for each LV as a whole is determined via a permutation test whereby the order of conditions is reassigned for each participant 1000 times without replacement. The number of times the permuted singular values exceed the observed singular values is calculated, providing exact probabilities for all LVs, and an objective means for determining the number of LVs to be retained. Because the decomposition of the data matrix is done in a single analytic step, correction for multiple comparisons is unnecessary.

The reliability of the weights (saliences) for the brain voxels showing the pattern of condition contrasts identified by the LVs is determined via bootstrap estimation of the standard errors in which participants are randomly re-sampled 1000 times with replacement. The salience/standard error ratio (bootstrap ratio) is analogous to a Z score that is used for thresholding images and creating activation maps. We used a bootstrap ratio of 3.3 (corresponding to $p < .001$) as a threshold. Local maxima for the brain areas with reliable saliences on each LV were defined as the voxel with a bootstrap ratio higher than any other voxel in a 2 cm cube centered on that voxel. To determine cluster location via Talairach atlas, PLS image coordinates were converted from Montreal Neurological Institute (MNI) space to Talairach coordinates using GingerALE Version 2.1.1. (http://www.brainmap.org/ale/). Multiplication of each voxel's salience by its BOLD signal intensity and summing across voxels for a given participant yielded a brain score that indicated the degree to which that participant expressed the activation pattern identified by the LV at each lag (TR). Given the z-shimming acquisition, each TR, beginning with the onset of the recording and ending just before the recording ended, was 4 s.

Mean-centered task PLS was used to determine the effect of memory age and vividness on distributed activation patterns at each lag. We first examined all autobiographical conditions compared to baseline, followed by task PLS analyses exploring the commonalities and distinctions among the three autobiographical conditions without considering the baseline.

In spatiotemporal seed PLS, condition specific correlations are computed between activation in a selected seed region of interest and the rest of the brain to derive the co-activation of the seed region with brain-wide activity across the design contrasts and lags. Given our theoretical interest in the hippocampus, we probed the involvement of this region in the autobiographical conditions. Specifically, we examined the left anterior hippocampus, given its central involvement in autobiographical memory (Gilboa et al., 2004; Söderlund et al., 2012; Svoboda and Levine, 2009). To extract a hippocampal cluster or voxels of interest unbiased with respect to condition, we performed a univariate analysis with AFNI, using a hippocampal mask, contrasting all autobiographical conditions from baseline, and selected the most significant voxels in the left anterior hippocampus that were involved in all conditions and survived a threshold of $p < 0.005$.

Results

Behavioural results

For each participant, the median vividness rating split remote/old memories into high and low vivid categories. Highly vivid old memories (high-old) had an average rating of 7.9 (SD = 1.4) and old memories that were not recalled as vividly (low-old) had an average rating of 4.8 (SD = 1.7), resulting (by design) in a significant difference in vividness ($t(9) = 13.350$, $p = 0.000$; all p-values are based on 2-tailed tests). Low-old memories were rated as less vivid compared to new memories ($t(9) = 6.59$, $p = 0.000$). Differences in rated vividness between the high-old memories and recent (new) memories fell just shy of statistical significance (new mean = 8.8, SD = 0.8; $t(9) = 2.12$, $p = 0.06$). As will be seen later, we nonetheless found

Table 1
Mean participant ratings of memories at time of encoding (when recording was made) and at the time of retrieval (when in the scanner). Standard deviations are in parenthesis.

	Encoding					Retrieval
	Memory age	Novelty	Importance	Emotion	Sum	Vividness
New	32 (14)[a]	2.5 (0.5)[a]	1.7 (0.5)[a]	1.8 (0.4)[a]	5.9 (0.7)[a,b]	8.8 (0.8)
High-old	546 (170)	3.1 (0.5)	2.4 (0.4)	2.6 (0.4)	8.0 (1.0)	7.9 (1.4)
Low-old	562 (165)	2.7 (0.4)	2.3 (0.5)	2.4 (0.4)	7.4 (1.1)	4.8 (1.7)[a]

[a] Significantly different from other conditions.
[b] Sum score = (novelty score + importance score + emotion score).

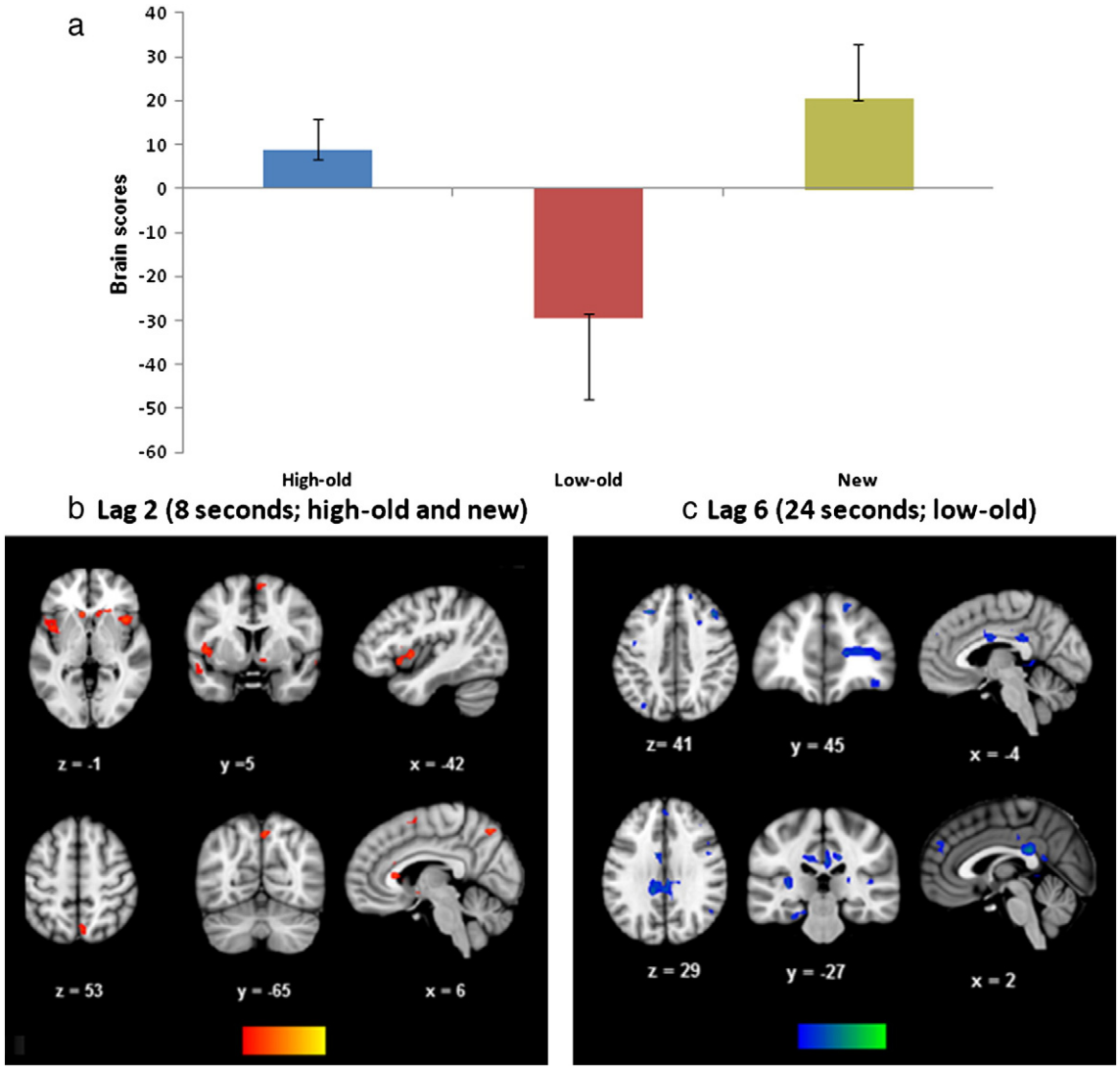

Fig. 1. Mean-centered task PLS. a.) The mean brain scores (summed scores of activity across the whole brain for each participant across all lags) from latent variable (LV) 1 with 95% confidence intervals that differentiated the high-old from the new and low-old conditions. The high-old and new conditions were associated with positive brain scores, whereas the low-old condition was associated with negative brain scores. Brain activity patterns associated with the two patterns at representative lags are presented in panel. b.) For high-old and new conditions at lag 2 and panel. c.) For low-old condition at lag 6. The figures are presented in MNI atlas space (see Tables 2a and 2b for full list of brain regions).

that the neural correlates of these memories were strongly modulated by vividness.

As noted in the methods, at the time of encoding, participants rated novelty, importance, and emotional change. There were significant differences between the memory conditions for each of these ratings (Novelty: $F(2,12) = 13.672$, $p = 0.001$; Importance: $F(2,12) = 7.428$, $p = 0.008$; Emotion; $F(2,12) = 7.804$, $p = 0.007$; Sum: $F(2,12) = 14.4221$, $p = 0.001$; see Table 1). These differences were driven by new events being rated as less novel, important, and emotional than the old events, most likely because these were sampled over a shorter

Table 2a
Reliable clusters identified for the first significant LV in the mean-centered task PLS across lags contrasting the three memory conditions across lags that were associated with the new and high-old memories (positive bootstrap ratios; BSR). Coordinates are in MNI space. Minimum cluster size was set at 10 voxels (voxel size = 4 × 4 × 4 mm).

Lag	Lobe	Brain structure	Brodmann area	X(mm)	Y(mm)	Z(mm)	BSR	Cluster size
1	Frontal lobe	Right superior frontal gyrus	9	24	52	28	5.6353	11
	Sub-lobar	Right thalamus	–	4	−68	52	5.9542	12
	Limbic lobe	Left hippocampus	–	−44	−20	−16	5.6982	10
2	Frontal lobe	Right medial frontal gyrus	6	8	4	64	4.6394	14
	Limbic lobe	Left parahippocampal gyrus	30	−28	−52	12	6.0779	13
	Sub-lobar	Right lentiform nucleus	–	12	4	−8	5.4978	20
		Left claustrum/insula	–	−36	0	4	5.5826	82
		Right caudate/insula	–	12	20	4	7.4763	140
	Parietal lobe	Right precuneus	7	4	−68	52	5.9542	12
3	Parietal lobe	Left precuneus	7	−4	−60	52	5.8031	51
5	Sub-lobar	Left insula	13	−48	4	−4	5.2665	14
7	Sub-lobar	Right insula	–	44	16	−4	4.9935	10

Table 2b
Reliable clusters identified for the first significant LV in the mean-centered task PLS contrasting the three memory conditions across lags that were associated with the low-old memories (negative bootstrap ratios; BSR). Coordinates are in MNI space. Minimum cluster size was set at 10 voxels (voxel size = 4 × 4 × 4 mm).

Lag	Lobe	Brain structure	Brodmann area	X(mm)	Y(mm)	Z(mm)	BSR	Cluster size
3	Temporal lobe	Right fusiform gyrus	37	52	−44	−8	−5.0778	38
	Midbrain	Left midbrain	Substania nigra	−8	−20	−12	−4.6252	10
	Parietal lobe	Left precuneus	31	−16	−40	36	−4.1872	13
	Posterior lobe	Left declive	–	−32	−80	−12	−5.4262	26
4	Frontal lobe	Right middle frontal gyrus	10	40	40	12	−6.5981	15
		Right middle frontal gyrus	8	36	36	40	−4.2476	12
	Limbic lobe	Left perirhinal cortex	–	−36	−44	−24	−5.2836	11
		Left cingulate gyrus	24	−24	−8	40	−7.4323	16
		Right cingulate gyrus	32	28	16	44	−4.3136	12
	Sub-lobar	Right thalamus	Pulvinar	24	−28	12	−8.7949	24
		Left insula	13	−32	−16	20	−4.8913	12
	Midbrain	Left midbrain	Red nucleus	0	−20	−16	−5.8991	16
	Temporal lobe	Right middle temporal gyrus	22	60	−44	0	−4.8218	13
		Right fusiform gyrus	–	28	−44	−28	−5.8009	11
	Parietal lobe	Left precuneus	7	−28	−64	40	−5.9626	23
	Posterior lobe	Left cerebellum	–	−28	−68	−12	−8.1194	63
		Left cerebellum	–	−24	−76	−32	−7.2009	15
		Left cerebellum	–	16	−40	−52	−5.9729	23
5	Frontal lobe	Right middle frontal gyrus	10	36	44	8	−8.4122	27
		Left precentral gyrus	4	−36	−20	60	−6.6223	10
		Right middle frontal gyrus	9	36	20	24	−6.1942	13
		Right middle frontal gyrus	8	44	28	44	−6.0543	17
		Right middle frontal gyrus	47	48	40	−16	−5.6915	12
		Left middle frontal gyrus	6	−32	16	48	−4.7992	10
		Right precentral gyrus	6	52	4	24	−4.0355	16
	Sub-lobar	Left caudate	Caudate tail	−12	−28	28	−7.2752	12
		Right insula	13	60	−36	16	−6.0451	11
		Right insula	13	48	−20	0	−5.6748	16
	Temporal lobe	Right middle temporal gyrus	–	60	−48	−4	−5.7221	12
	Parietal lobe	Right supramarginal gyrus	40	48	−36	32	−4.8831	22
	Posterior lobe	Left inferior semi-lunar lobule	–	−20	−80	−36	−6.1292	15
6	Frontal Lobe	Left middle frontal gyrus	8	−28	28	40	−8.8053	34
		Right superior frontal gyrus	8	16	44	44	−7.539	10
		Right middle frontal gyrus	6	44	20	44	−7.3455	32
		Right medial frontal gyrus	9	16	48	8	−6.8316	88
		Right medial frontal gyrus	32	24	16	40	−5.9591	24
		Right precentral gyrus	6	48	4	28	−5.6761	31
		Right precentral gyrus	13	56	−8	8	−5.3649	28
		Left precentral gyrus	4	−32	−16	56	−5.3164	13
		Left precentral gyrus	6	−44	−4	44	−5.207	10
		Left medial frontal gyrus	9	0	52	28	−5.0906	22
		Right middle frontal gyrus	11	36	44	−12	−4.8701	10
	Limbic lobe	Left posterior cingulate	23	0	−36	24	−7.6494	126
		Left hippocampus	–	−28	−24	−20	−6.259	25
		Left cingulate gyrus	24	−8	4	28	−6.0242	23
	Sub-lobar	Right thalamus	Pulvinar	24	−24	12	−7.6634	17
		Right insula	13	52	−8	20	−5.04	14
	Temporal lobe	Left caudate	Caudate tail	−32	−28	4	−6.6905	13
		Right middle temporal gyrus	39	52	−60	28	−6.0143	31
		Right superior temporal gyrus	39	56	−52	8	−5.7854	19
		Right middle temporal gyrus	21	60	−16	−12	−5.7015	10
	Occipital lobe	Left superior occipital gyrus	19	−36	−76	36	−6.5366	12
	Posterior lobe	Left cerebellum	–	−20	−80	−36	−7.6933	20
		Right cerebellum	–	20	−52	−44	−6.8945	40
		Left cerebellum	–	−16	−72	−16	−5.626	10
		Left cerebellum	–	−28	−84	−16	−5.0078	15
		Right cerebellum	-	36	−64	−16	−4.6997	10
7	Frontal lobe	Right middle frontal gyrus	8	40	24	40	−9.1897	87
		Right medial frontal gyrus	9	28	40	12	−7.7685	102
		Left middle frontal gyrus	8	−24	28	40	−4.7012	15
	Limbic lobe	Left posterior cingulate	29	0	−40	24	−13.193	66
		Left posterior cingulate	29	−4	−52	12	−5.1166	31
	Sub-lobar	Left insula	13	−48	−36	20	−6.6365	15
		Left thalamus	Pulvinar	−28	−24	8	−5.0056	11
	Temporal lobe	Left superior occipital gyrus	39	−32	−76	36	−5.6416	10
	Parietal lobe	Right inferior parietal lobule	40	56	−28	24	−5.105	48
		Left postcentral gyrus	3	−28	−24	44	−4.8423	36
		Right superior parietal lobule	7	28	−56	44	−4.6574	10
		Right supramarginal gyrus	40	44	−40	32	−4.4016	11
		Left inferior parietal lobule	40	−64	−28	36	−4.3622	11
	Occipital lobe	Left cuneus	19	−8	−80	44	−4.15	17
	Posterior lobe	Right cerebellum	–	32	−68	−16	−4.0431	16

time frame with less significant events available for selection. Although these new events were deemed less significant at encoding than old events, their ratings of vividness at retrieval were uniformly high. There were no significant differences for the encoding ratings between high- and low-old events, confirming the equivalence of these events at the time of encoding.

Functional results

Task PLS

An initial mean-centered PLS analysis with high-old, low-old, new and the baseline (reversed speech) conditions revealed a significant LV that dissociated all the autobiographical memory conditions from the baseline task ($p < 0.000$, 55.11% of the cross-block variance accounted for). Revealing the similarities in brain activity between all three autobiographical conditions, this LV included core regions in the autobiographical memory network (Maguire, 2001; Svoboda et al., 2006) including bilateral middle and medial prefrontal cortices, posterior cingulate, the middle, superior and medial temporal gyri, including the hippocampus and parahippocampal gyri, and posterior regions, such as the left precuneus, right cuneus and the bilateral cerebellum (Supplementary Table 1).

Because we were interested in exploring the differences between the memory conditions, we ran a mean-centered PLS excluding the baseline condition. One significant LV dissociated the high-old and new conditions from the low-old condition ($p < 0.001$, 61.02% of the cross-block covariance accounted for; see Fig. 1a). The high-old and new conditions were associated with right superior and medial frontal, right precuneus, left insula, bilateral thalamic, and left parahippocampal activity at lag 2, then decreasing (see Fig. 1b and Table 2a). The low-old condition was associated with left middle and posterior cingulate, left and right precentral, right middle and medial frontal, left hippocampal, bilateral middle and superior temporal, cerebellar, and bilateral thalamic activity appearing first at lag 3 and then increasing in strength (see Fig. 1c and Table 2b).

Spatiotemporal seed PLS

A left hippocampal seed voxel was selected from a separate univariate analysis, unbiased with respect to condition and time. We chose a voxel in the anterior hippocampus (MNI = −20, −2, −17) and extracted percent signal change from an 8 mm sphere around that seed across lags from the first mean-centered PLS that reported similar brain regions in all three autobiographical conditions.

Fig. 2 displays the mean percent signal change in the anterior hippocampal seed across lags. While all three conditions reached comparable levels of activity in this left hippocampal seed, the conditions were associated with different patterns of activation over the retrieval period. This is confirmed by a significant interaction of condition and time ($F(12,108) = 1.827$, $p = .05$), but no significant main effect of condition ($F(2,18) = 1.299$, $p = .297$) or time ($F(6,54) = .655$, $p = .686$). Follow-up analyses of the simple effect of condition indicated that activity in the low-old condition was significantly different from the high-old condition at lag 7 ($t(9) = 4.217$, $p = 0.002$) and from the new condition at lags 6 and 7 ($t(9) = 3.259$, $p = .01$; $t(9) = 2.922$, $p = .017$).

This left anterior hippocampal seed was entered into the seed PLS analysis to explore its connectivity across three autobiographical retrieval conditions. Two significant LVs were found. The first LV ($p < 0.000$, accounting for 42.82% of the cross-block covariance) dissociated the high-old from the low-old conditions in relation to the new condition across time. As seen in Fig. 3 and Table 3, the new condition was associated with sustained hippocampal–neocortical connectivity across lags, whereas the high- and low-old conditions showed discrepant patterns that can be discerned by examining 95% confidence intervals around the correlations; those that do not cross zero are significant. During early lags (1–3), there was co-activation

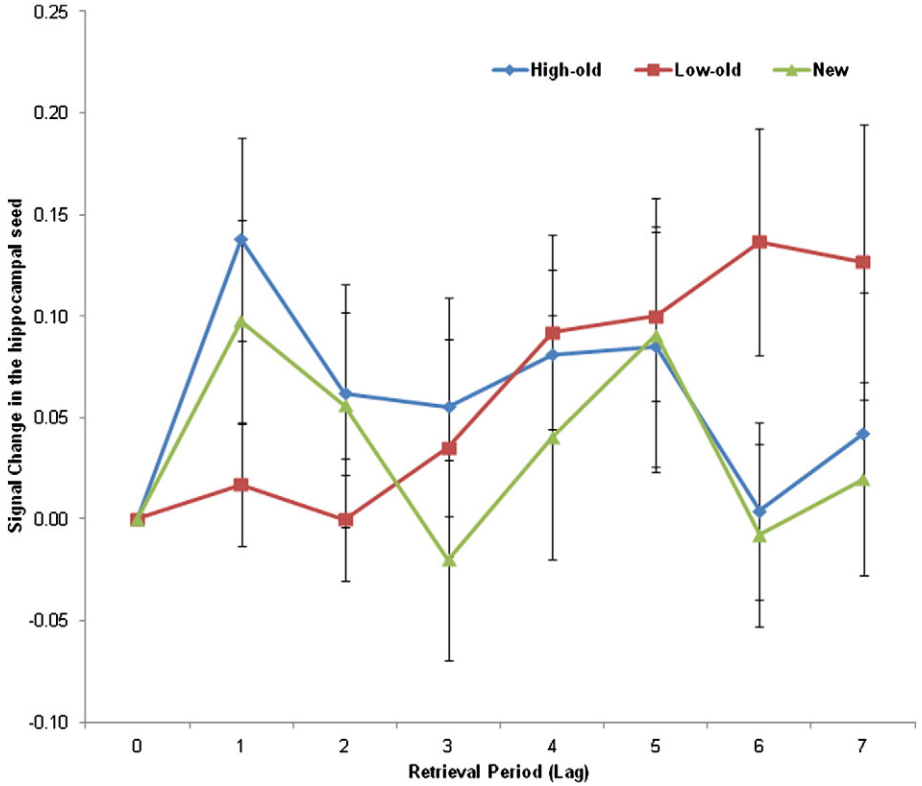

Fig. 2. The mean percent signal change of a left anterior hippocampal seed at MNI coordinates −21, −2, and −17 across the three retrieval conditions and lag. Error bars indicate standard error of the mean.

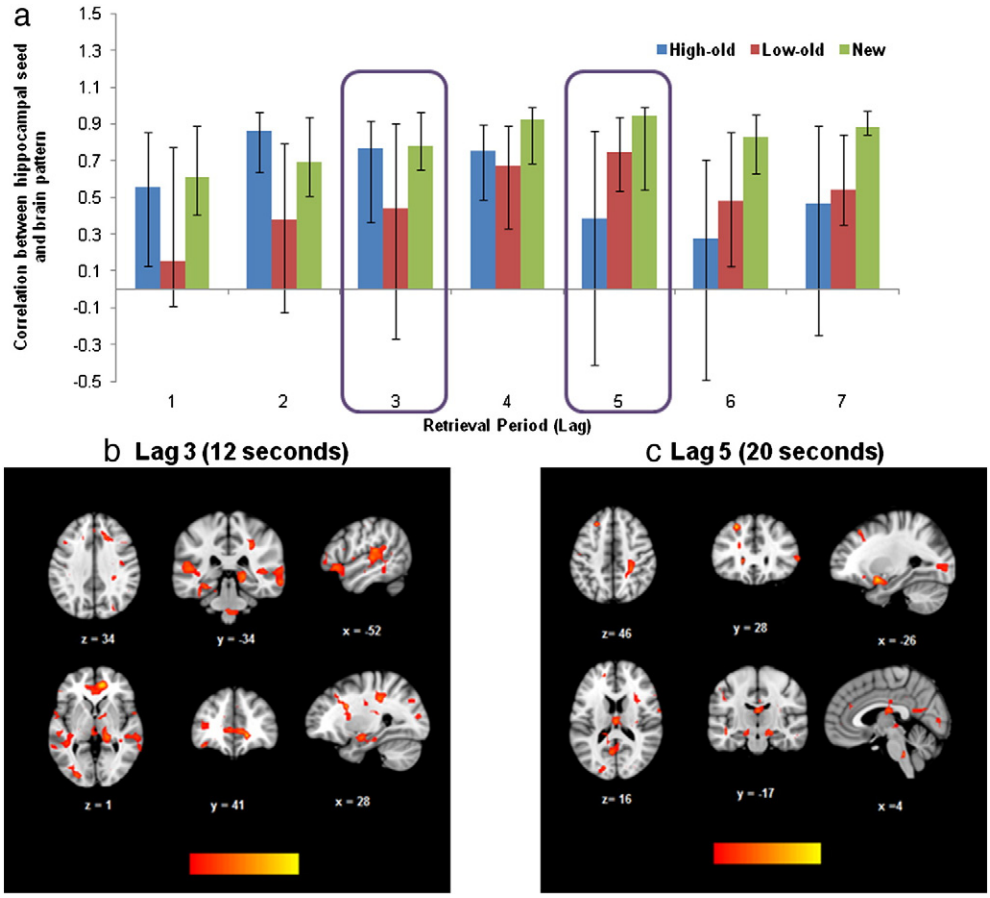

Fig. 3. Seed PLS results depicting cortical connectivity with a left anterior hippocampal seed for the three conditions. a) Correlation between the seed and the brain pattern as a function of memory condition (bar color) and time (lags 1 to 7). b) Patterns of connectivity for the early retrieval period (lag 3) associated with the high-old and new memories. c) Patterns of connectivity for the later retrieval period (lag 5) associated with the low-old and new memories. The connectivity patterns depicted represent clusters that survive a bootstrap ratio > 5.0 and a cluster size greater than 10 voxels (see Table 3 for full list of clusters). Error bars represent 95% confidence intervals.

with the left anterior hippocampus and the left inferior frontal gyrus, the left superior frontal gyrus, right insula, the cingulate gyrus bilaterally, the middle temporal gyrus bilaterally, the left precuneus, the lingual gyrus bilaterally, and the left cerebellum for the high-old and new memories. During later lags, the hippocampus was co-activated with the inferior frontal and middle frontal gyrus bilaterally, the cingulate bilaterally (anterior and posterior), the superior temporal gyrus bilaterally, the left thalamus, the lingual gyrus bilaterally, and the right hippocampus for low-old and new memories.

The second LV ($p < 0.024$; accounting for 21.93% of the variance; Fig. 4), separated the connectivity patterns associated with the old (high and low) conditions from the new condition. For middle lags (3–5) old memories were associated with hippocampal–neocortical connectivity distributed in the right middle, superior and medial frontal gyrus, left precentral gyrus and regions of the right precental gyrus, left superior temporal lobe and left cerebellum, whereas new memories were associated with hippocampal connectivity to the right precuneus, left hippocampal regions (posterior), cingulate and caudate.

Discussion

The contrast of recent and remote events in autobiographical memory research is confounded by the inherent differences in these events, such as vividness and rehearsal. This study reduced these confounds by using highly potent, prospectively collected retrieval cues that were effective in eliciting vivid recollection of recent and remote events that were unique, but not significant enough to be readily accessible to uncued free recall. We were therefore able to study events clearly separated into two time periods that cannot usually be resolved through a retrospective cueing method, but which nonetheless reflect an important period of memory transformation (Addis et al., 2004; Bontempi et al., 1999; Remondes and Schuman, 2004; Rubin and Schulkind, 1997a, 1997b; Söderlund et al., 2012). While retrospective cues are advantageous for neuropsychological and neuroimaging investigations, a drawback of these methods is the lack of control over characteristics differentiating remote from recent memories (e.g., vividness, importance, emotionality, novelty). As the retrieval cues were collected prospectively for everyday events, such biases were well controlled, allowing us to examine vividness independently from memory age.

Using multivariate analysis, we examined the spatiotemporal patterns of neural activity (Task PLS; Fig. 1) associated with memory retrieval across the three conditions (recent, remote (old) vivid and remote (old) non-vivid memories). This analysis revealed a pattern of activity that dissociated vivid and non-vivid memories, irrespective of memory age. Vivid memories were associated with activity in right frontal, left insula and hippocampus, bilateral posterior (precuneus, angular gyrus), caudate, and thalamic regions, whereas non-vivid memories were associated with more expansive activity appearing at relatively later lags, particularly in the left cingulate, right middle frontal, and right superior and middle temporal gyrus, as well as the lateral and posterior regions of the thalamus.

These results were robust even though the sample size was relatively small, as necessitated by the intense demands on participants

Table 3
Reliable clusters that co-varied with the left anterior hippocampal seed (MNI coordinates = −20, −2, −17) for LV1 at lag 3 (the most robust correlations occurred for new and high-old memories; low-old memories did not contribute) and at lag 5 (the most robust correlations occurred for new and low-old memories; high-old did not contribute). BSR refers to bootstrap ratios. Minimum cluster size was set at 10 voxels (voxel size = 4 × 4 × 4 mm).

Lag	Lobe	Brain structure	Brodmann area	X(mm)	Y(mm)	Z(mm)	BSR	Cluster size
3	Frontal lobe	Left superior frontal gyrus	8	−20	28	40	6.1521	15
		Left inferior frontal gyrus	47	−52	24	−8	6.0824	59
		Left middle frontal gyrus	9	−40	16	28	5.2529	51
		Right middle frontal gyrus	6	36	16	48	4.6171	12
		Left paracentral lobule	31	0	−24	48	4.441	17
	Limbic lobe	Right anterior cingulate	32	16	44	−4	12.6719	165
		Left parahippocampal gyrus	34	−28	4	−20	8.7535	209
		Right parahippocampal gyrus	28	20	−16	−16	8.5913	721
		Right cingulate gyrus	31	28	−32	36	6.7088	72
		Left posterior cingulate gyrus	23	−4	−60	20	6.1461	26
		Right cingulate gyrus	24	8	−8	44	5.8469	56
		Left cingulate gyrus	32	−12	20	20	4.6719	21
	Sub-lobar	Right insula	13	36	8	16	12.302	232
		Right insula	13	52	−24	24	5.1043	49
	Temporal lobe	Right middle temporal gyrus	21	64	−32	−12	6.7069	129
		Left superior temporal gyrus	22	−56	0	4	6.0166	18
		Right superior temporal gyrus	38	56	8	−20	5.9517	15
		Right superior temporal gyrus	22	56	−16	−16	5.6979	19
		Right supramarginal gyrus	40	64	−48	24	5.4909	35
	Parietal lobe	Left postcentral gyrus	2	−44	−20	52	6.6825	52
		Left precuneus	7	−24	−44	48	4.642	10
		Left precuneus	19	−32	−68	40	4.0203	18
	Occipital lobe	Left lingual gyrus	17	−24	−92	4	6.8289	90
		Right lingual gyrus	–	24	−80	4	6.7143	28
		Right cuneus	18	12	−80	28	5.3665	12
		Right precuneus	31	28	−76	36	4.4501	10
	Posterior lobe	Left cerebellum	–	−28	−72	−28	8.9355	12
		Left cerebellum	–	−4	−72	−28	5.3882	20
5	Frontal lobe	Left inferior frontal gyrus	34	−24	4	−16	12.6845	90
		Right precentral gyrus	6	60	4	8	6.4609	22
		Right middle frontal gyrus	46	56	36	12	6.0459	22
		Left inferior frontal gyrus	47	−32	24	−16	5.4737	14
		Left middle frontal gyrus	8	−24	28	48	10.4947	32
		Left medial frontal gyrus	9	−16	48	20	7.4824	17
		Right paracentral lobule	5	28	−36	48	7.2097	79
	Limbic lobe	Left posterior cingulate	30	−4	−48	24	6.413	111
		Right anterior cingulate	32	16	44	−4	5.0672	12
		Right parahippocampal gyrus	–	24	−4	−20	4.5888	22
		Left cingulate gyrus	32	0	36	28	4.0017	10
		Right hippocampus	–	40	−8	−20	5.9417	19
	Sub-lobar	Left caudate	–	−16	28	0	6.4761	16
		Left thalamus	–	0	−16	16	6.0164	68
		Left thalamus	–	0	−28	0	5.167	19
	Temporal lobe	Left fusiform gyrus	21	−44	−16	−12	6.3693	20
		Right superior temporal gyrus	41	60	−24	4	5.3184	21
		Left superior temporal gyrus	22	−60	−28	4	4.8278	12
		Left fusiform gyrus	37	−44	−64	−12	4.2502	11
	Midbrain	Right midbrain	–	12	−20	−12	6.7517	19
	Occipital lobe	Right lingual gyrus	17	16	−88	8	6.3652	19
		Left lingual gyrus	18	0	−80	0	6.02	15
	Parietal lobe	Left postcentral gyrus	2	−52	−16	48	4.7392	25
	Posterior lobe	Left cerebellum	–	−16	−84	−16	6.4233	115
		Right cerebellum	–	40	−76	−28	6.3307	66
		Right cerebellum	–	28	−72	−36	4.2619	11

(i.e., the collection of prospective cues over the course of one to two years), which speak to the potency of our retrieval cues. Further, the reported division between vivid and non-vivid memories was evident even though vivid remote and recent memories were not evenly matched for vividness ratings (recent memories were slightly more vivid, on average). Had these ratings been better matched, we expect we would have gotten even stronger overlap between recent and remote vivid memories. We cannot rule out the possibility that a larger sample would have revealed differences between vivid remote and recent memories. Such a finding, however, would not speak against the main findings of hippocampal involvement across condition and a dissociation of non-vivid remote memories.

From a general perspective, these findings from our task PLS analysis extend previous reports of hippocampal involvement in memory regardless of age, supporting the Multiple Trace Theory (Bonnici et al., 2012; Maguire, 2001; Moscovitch, 2008; Nadel et al., 2000; Piolino et al., 2004; Rekkas and Constable, 2005; Viard et al., 2007). While most prior studies of memory remoteness involve lower temporal resolution due to the use of retrospective retrieval cues, animal studies using experimentally-manipulated cues demonstrate that crucial elements of consolidation occur within shorter time frames that, when extrapolated to humans, are within the 1–2 year delay employed in this study (Anagnostaras et al., 1999; Bontempi et al., 1999; Remondes and Schuman, 2004; Winocur et al., 2005). Nonetheless, these results do not address potential consolidation processes occurring greater than 1.5 years post-encoding.

These findings suggest different routes or processes used to retrieve autobiographical memories (Addis et al., 2012). Memories

Table 4
Reliable clusters that co-varied with the left anterior hippocampal seed (MNI coordinates = −20, −2, −17) for LV2 at lags 2, 3, and 4. Negative bootstrap ratios (BSR) are associated with the new condition and positive bootstrap ratios are associated with the high-old and low-old condition. Coordinates are in MNI space. Minimum Cluster Size was set at 5 voxels (voxel size = 4 × 4 × 4 mm).

Lag	Lobe	Brain structure	Brodmann area	X(mm)	Y(mm)	Z(mm)	BSR	Cluster size
Negative BSRs								
2	Frontal lobe	Left medial frontal gyrus	8	−8	48	36	−5.7683	6
		Left superior frontal gyrus	6	−12	28	56	−4.9337	11
		Right middle frontal gyrus	10	32	44	8	−4.4883	8
	Limbic lobe	Right hippocampus	–	28	−16	−24	−5.1653	8
3	Temporal lobe	Left hippocampus	–	−32	−44	4	−5.9044	18
	Limbic lobe	Left cingulate gyrus	31	−8	−24	44	−5.4349	11
	Sub-lobar	Left caudate	Caudate tail	−24	−40	20	−5.433	10
		Left claustrum/insula	-	−24	12	20	−4.4041	6
4	Limbic lobe	Left cingulate gyrus	24	−4	4	20	−4.6252	7
Positive BSRs								
2	Frontal lobe	Right precentral gyrus	6	16	−12	68	51.5977	12
	Limbic lobe	Left Cingulate Gyrus	2	−20	−20	40	4.6752	7
	Temporal lobe	Right superior temporal gyrus	–	60	4	−8	4.697	10
3	Anterior lobe	Left culmen	–	−36	−36	−28	4.1866	5
	Frontal lobe	Left precentral gyrus	6	−60	4	8	4.0489	6
		Right superior frontal gyrus	9	20	48	32	4.5294	7
		Right medial frontal gyrus	6	8	4	56	5.6941	6
		Right middle frontal gyrus + precentral gyrus	6	36	−4	48	7.0135	39
	Sub-lobar	Right insula	13	44	−12	12	4.2212	15
		Left lentiform nucleus	Putamen	−20	4	−8	4.8878	12
	Parietal lobe	Right precuneus	7	16	−44	64	3.7254	5
		Right postcentral gyrus	2	36	−20	36	4.3296	6
		Right postcentral gyrus	2	40	−32	32	5.9489	8
	Posterior lobe	Left cerebellum	–	−24	−72	−28	4.2382	6
	Temporal lobe	Left superior temporal gyrus	22	−56	−12	4	3.798	9
		Right superior temporal gyrus	22	60	12	−4	6.0563	25
4	Frontal Lobe	Right superior frontal gyrus	9	−44	−60	−32	4.1823	6
		Right medial frontal gyrus	10	24	52	28	4.4268	11
		Right superior frontal gyrus	10	8	64	12	4.7886	5
		Left superior frontal gyrus	10	24	56	8	4.8521	14
		Right precentral gyrus	44	−16	60	8	5.0558	11
		Left middle frontal gyrus	6	60	12	0	5.4782	10
		Right medial frontal gyrus	6	−32	4	60	8.1602	73
	Limbic lobe	Left posterior cingulate	23	8	4	56	4.4873	14
		Right parahippocampal gyrus	30	0	−60	20	4.5357	7
		Left parahippocampal gyrus	35	12	−40	0	5.1443	12
	Sub-lobar	Right caudate	Caudate head	−24	−28	−28	6.7828	28
	Temporal lobe	Left superior temporal gyrus	22	16	20	−4	4.2367	5
		Right superior temporal gyrus	38	−56	−16	0	7.9484	5
	Parietal lobe	Left inferior parietal lobule	40	60	4	−12	4.0273	6
		Left precuneus	7	−48	−32	52	5.2001	14
		Right precuneus	7	−8	−52	64	5.9904	46
		Left inferior parietal lobule	40	8	−44	52	6.1212	27
		Right sub-gyral	40	−48	−48	40	7.0391	229
	Posterior lobe	Left cerebellar tonsil	–	28	−40	56	4.1986	9
		Right cerebellar tonsil	–	−4	−48	−48	4.9286	14
	Occipital lobe	Left middle occipital gyrus	19	8	−64	−40	5.326	9
		Left lingual gyrus	18	−44	−80	12	6.9888	218
	Anterior lobe	Right culmen	–	−4	4	20	4.5282	5
		Left nodule	–	48	−44	−24	4.5343	12
		Left culmen	–	0	−60	−28	8.269	89

can be accessed either directly or through generative processes. We found that while both vivid and non-vivid memories engaged key regions of the autobiographical network (Supplementary Table 1), vivid memories were associated with a quick onset of activity that was more focused in medial regions and posterior parietal regions, which likely reflect a direct mode of retrieval and the absence of a protracted search and rapid reintegration of the details stored in posterior regions of the brain (Cabeza and St Jacques, 2007; Nadel et al., 2000; Svoboda et al., 2006). Non-vivid memories, on the other hand, were associated with more expanded neural activity, particularly in frontal regions (e.g., bilateral superior and middle frontal gyri). As predicted, this likely reflects a more effortful or generative mode of retrieval that must occur before specific detailed information is accessed. Accordingly, we found that activity in a left hippocampal seed was greater for non-vivid remote memories compared to both recent and remote vivid memories (Fig. 2), perhaps because the initial retrieval time was devoted to neocortically-mediated generative processes. In contrast to a recent study using very recent (2 weeks) versus remote (10 years) retrospectively collected memories matched for vividness (Bonnici et al., 2012), we did not find an effect of memory age along the long axis of the hippocampus, although the later peaks for low-vivid memories indicate a difference in temporal contribution of this hippocampal region that is dictated in part by vividness.

We further examined the neural context of these findings by assessing the functional connectivity between the hippocampus and the rest of the brain across memories with different characteristics (Figs. 3 and 4). We selected a left anterior hippocampal seed from a separate analysis of retrieval activation, which was proximal to hippocampal peaks in other studies of autobiographical memory (Gilboa et al., 2004; Söderlund et al., 2012). A pattern of co-activated cortical regions

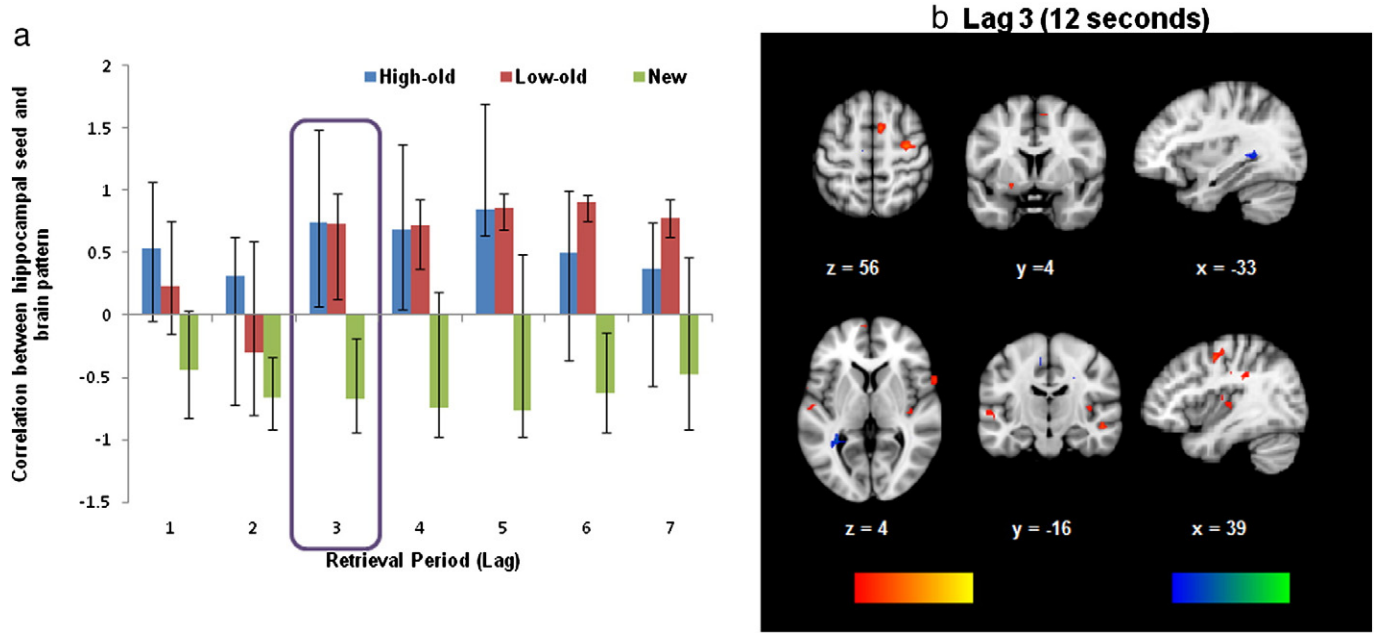

Fig. 4. The second significant LV for seed PLS with the anterior hippocampal seed as depicted in the early retrieval time period and later in the retrieval period. a.) Each bar plots the correlation with the brain pattern displayed as a function of memory condition (bar color) and time (lags 1 to 7). b.) The brain figure associated with functional connectivity at lag 3. Regions shown in cool colors are associated with negative brain scores, the new condition, and regions shown in warm colors are associated with the low-old and high-old conditions (see Table 4 for full list of clusters).

with the anterior hippocampus showed a rapid and early onset of activity in association with vivid memories, including the right inferior frontal gyrus, reflecting a quick recovery of autobiographical memory and specific event construction (Greenberg et al., 2005; Holland et al., 2011); posterior regions (e.g., inferior parietal lobule), possibly reflecting greater attention to the details of the event being recalled (Cabeza et al., 2008); and the precuneus as well as other regions of the posterior parietal cortex and occipital lobe (lingual gyrus), associated with imagery and re-experiencing (Cavanna and Trimble, 2006). Non-vivid memories were associated with later co-activation between the hippocampal seed and the posterior cingulate cortex, superior and middle temporal gyrus, frontal gyrus, and insula. The additional temporal cortical co-activation associated with these less vivid memories may reflect more semantic information being integrated alongside the episodic content of these events. This result, in conjunction with recent animal models, (e.g., Goshen et al., 2011) implicates a less direct, slower retrieval process to bind together details of a memory into a coherent autobiographical context when there is less vivid recall. In comparison to remote memories, recent memories were associated with sustained co-activation with the hippocampus throughout the retrieval period. We speculate that new memories, like vivid remote memories, are associated with direct retrieval (as supported by early hippocampal co-activation), but recent memories may have more details to bind to the directly accessed memory as time goes on (supported by later hippocampal co-activation). Further investigations are required to assess this possibility.

The contrasting spatiotemporal patterns associated with vivid memories and non-vivid memories fit with other investigations that have compared specific event retrieval to general event retrieval (Holland et al., 2011), with specific event retrieval associated with increased medial and dorsal prefrontal, MTL, and precuneus activity, reflecting increased recovery of details and vividness (Hennessey Ford et al., 2011). The present findings extend these results by using more specific retrieval cues of recent and remote events and by adding a temporal dimension. Perhaps for the non-vivid memories, like those in our study that had a later onset of hippocampal connectivity, retrieval can move from general to specific across the 30-second epoch. Participants may have inched closer to a threshold of re-experiencing that is likely reached at earlier time-points for vivid memories. In studies using less specific cues (e.g., pictures, event titles), earlier frontal activation can accompany initial search strategies for less vivid or more remote memories associated with effortful retrieval (Holland et al., 2011; Söderlund et al., 2012). Such activation was not observed in the present study as retrieval could occur through simply listening to the recording without engaging generative retrieval processes. Similarly, the direct, vivid retrieval for everyday events, as in the old-high condition could not have been obtained with the less specific cues used in most studies of autobiographical memory. In agreement with the present findings, using the same paradigm with magnetoencephalography (MEG), we found that increased theta phase coupling between the MTL and the medial prefrontal and precueus regions was correlated with vividness ratings (Fuentemilla et al., 2013). It remains to be seen whether these results would extend to more remote memories, although similar results were observed for retrospectively cued memories ranging from 1 month to 10 years of age (Söderlund et al., 2012).

Although our main findings emphasize the effects of vividness on hippocampal activity and connectivity when retrieving memories, we nonetheless found a pattern of hippocampal–neocortical connectivity that was specific to remote memories, regardless of vividness. This pattern was characterized by late and more robust onset activity of the autobiographical network (MTL, temporal, medial frontal and parietal regions) for remote relative to recent memories (Fig. 4). This may relate to differences at encoding between recent memories and remote memories, as indicated by lower ratings for novelty, importance, and emotional change for recent as compared to remote memories. However, we suspect a more parsimonious explanation that this pattern reflects a rapid recovery of details and re-experiencing associated with these very recent memories relative to remote memories. Indeed, these memories were vividly re-experienced in spite of being less significant, as indicated by the encoding ratings. These findings do not necessarily undermine the vividness effects, which were more statistically robust and observed for both connectivity and activation analyses. Rather, they suggest an additional advantage for very recent memories experienced days or weeks before scanning (relative to those experienced

many months before scanning) in the engagement of the autobiographical network. In fact, given their recency, it is remarkable that the high-old memories were relatively matched to them for both vividness and patterns of brain activity.

Conclusion

This study used an unbiased and novel method to capture autobiographical memory retrieval to reveal the critical influence of vividness in the underlying neural pattern and functional connectivity that is associated with remote and recent memories. That both recent and remote memories implicated the hippocampus, albeit a different network that depends on both vividness and age, has consequences for theories of memory, particularly consolidation. More work should be done to explore the interaction of vividness and memory age using memories from even more remote time periods using such prospective cues.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.neuroimage.2013.06.082.

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Conflict of interest statement

None of the authors have any conflicts of interest to state.

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