

Rapid Communication

**Representations of recent and remote
autobiographical memories in
hippocampal subfields**

Heidi M. Bonnici, Martin J. Chadwick and Eleanor A. Maguire¹

Wellcome Trust Centre for Neuroimaging, Institute of Neurology, University College
London, London WC1N 3BG, United Kingdom

¹Corresponding author:

e.maguire@ucl.ac.uk

T: +44-20-34484347

F: +44-20-78131445

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ABSTRACT: The hippocampus has long been implicated in supporting autobiographical memories, but little is known about how they are instantiated in hippocampal subfields. Using high resolution functional MRI combined with multi-voxel pattern analysis we found it was possible to detect representations of specific autobiographical memories in individual hippocampal subfields. Moreover, while subfields in the anterior hippocampus contained information about both recent (two weeks old) and remote (ten years old) autobiographical memories, posterior CA3 and DG only contained information about the remote memories. Thus, the hippocampal subfields are differentially involved in the representation of recent and remote autobiographical memories during vivid recall.

Key words: subfields; autobiographical; fMRI; MVPA; consolidation; hippocampus

There is wide agreement that the hippocampus is necessary for acquiring autobiographical memories, the memories of our personal past experiences, and for their recall in the short-term (Scoville and Milner, 1957). By contrast, there is less consensus about the hippocampal role in recollection of autobiographical memories that are more remote. The standard model of consolidation argues that declarative (including autobiographical) memories become less dependent on the hippocampus over time, eventually abjuring the need for its involvement during retrieval (Marr, 1971; Teyler and DiScenna, 1985; Squire, 1992). Alternative theories (Multiple Trace Theory, Scene Construction Theory) propose instead that the hippocampus is necessary for retrieving vivid autobiographical memories in perpetuity (Nadel and Moscovitch, 1997; Winocur and Moscovitch, 2011; Hassabis and Maguire, 2007, 2009). Differential findings across studies of amnesic patients with hippocampal lesions (reviewed in Winocur and Moscovitch, 2011), as well as disparate results from functional MRI (fMRI) experiments (e.g. Maguire et al., 2001; Ryan et al., 2001; Maguire and Frith, 2003; Gilboa et al., 2004; Piolino et al., 2004; Rekkas and Constable, 2005; Steinworth et al., 2006; Viard et al., 2007; Watanabe et al., 2012; but see Niki and Luo, 2002; Piefke et al., 2003) contribute to the impasse.

In a recent high resolution fMRI study, Bonnici et al. (2012a) availed themselves of the opportunity afforded by multi-voxel pattern analysis (MVPA; Haynes and Rees, 2006; Norman et al., 2006; Chadwick et al., 2012) to provide an alternative to conventional neuropsychological and fMRI approaches, by detecting representations of individual autobiographical memories in patterns of fMRI activity. They examined whether information about specific recent (two weeks old) and remote (ten years old) autobiographical memories was represented in the hippocampus. They found that information about both types of memory was detectable in the hippocampus, suggesting it plays a role in the retrieval of vivid autobiographical memories regardless of remoteness. Interestingly, they also reported that while recent and remote memories were both represented within anterior and posterior hippocampus, the latter nevertheless contained more information about remote memories. Thus, the hippocampus respected the distinction between recent and remote memories.

Functional differentiation down the long axis of the hippocampus has been documented in a range of species including humans (e.g. Moser and Moser, 1998; Maguire et al., 2000; Gilboa et al., 2004; Rekkas and Constable, 2005; Fanselow and Dong, 2010; Poppenk and

Moscovitch, 2011; Ranganath and Ritchey, 2012; for a recent review see Poppenk et al., 2013). Bonnici et al.'s (2012a) findings clearly prompt further questions about what might be occurring within anterior and posterior hippocampus during autobiographical memory recall. But there is also another parcellation of the hippocampus that needs to be considered. The hippocampus is composed of a number of subregions CA1, CA2 and CA3 (Lorente de No, 1934), bordered by the dentate gyrus (DG) and subiculum (Amaral and Lavenex, 2007). The findings of Bonnici et al. (2012a) gave no indication as to whether their anterior/posterior differential effects were being driven by all subfields, or by one or two in particular. Studies in rodents and computational models suggest that key computations necessary for memory occur in the subfields, such as pattern separation (in DG and CA3), the process of distinguishing similar memories from each other, and pattern completion (in CA3), which facilitates the retrieval of previously stored memories from partial cues (Kesner et al., 2004; Leutgeb et al., 2004, 2007; Leutgeb and Leutgeb, 2007; Alvernhe et al., 2008; Hunsaker and Kesner, 2008; Gilbert and Brushfield, 2009; Aimone et al., 2011; Marr, 1971; Treves and Rolls, 1994; McClelland et al., 1995; Rolls, 2010; O'Reilly et al., 2011). To date only one study has explored autobiographical memory in relation to the hippocampal subfields. Bartsch et al. (2011) reported that patients with transient global amnesia had apparently focal lesions in CA1 and a concomitant impairment in recalling both recent and remote autobiographical memories. However, focal lesions to other subfields were not examined in this study, so it is unknown whether CA1 is particularly critical for autobiographical memory retrieval, or if a lesion to any subfield would be sufficient to disrupt processing within the hippocampus leading to autobiographical memory recall deficits.

Given the dearth of knowledge about the role of hippocampal subfields in supporting autobiographical memory retrieval, in this study we set out to address three issues that have not been investigated before. First, using high resolution structural and functional MRI combined with MVPA we sought to ascertain if information about individual autobiographical memories could be detected in specific hippocampal subfields of healthy participants. If so, we aimed to examine whether recent and remote autobiographical memories were differentially represented in those subfields. Third, considering the results of Bonnici et al. (2012a), we also investigated how representations of the memories related to a subfield's anterior or posterior hippocampal location.

A prerequisite for our study was the ability to delineate the subfields. We followed a recently-published scanning and subfield segmentation protocol that allowed us to manually identify and separate CA1, CA3 (which also included CA2), DG and subiculum (Bonnici et al., 2012b). This required high resolution T2-weighted structural MR images acquired on a 3T MRI scanner with an isotropic voxel resolution of 0.5x0.5x0.5mm focused on the medial temporal lobes (see Supporting Online Material for details). Given that sets of these scans were available for the participants in the Bonnici et al. (2012a) study of autobiographical memories, we identified CA1, CA3, DG and subiculum in each of these participants (Fig. 1), and then re-analyzed the fMRI data from that study, this time focusing our MVPA analyses on the hippocampal subfields.

The participants were 12 healthy right-handed, university-educated subjects (9 female; mean age 27.5 years, SD 3.2, range 22-33). All gave informed written consent to participation in accordance with the local research ethics committee. Autobiographical memories were elicited one week before scanning (see Bonnici et al., 2012a for full details, and also Supporting Online Material). Recent and remote memories were closely matched on factors such as vividness, level of detail, emotional valence, ease of recall, and frequency of retrieval since the initial episode (see Table S1 in Supporting Online Material). This was important in order to rule out differences in these basic variables as driving differential effects that might be detected in the fMRI analyses. One week later, participants were scanned using high resolution (1.5mm³ isotropic voxels) fMRI scanning on a 3T MRI scanner (see Supporting Online Material for details) while they recalled 6 autobiographical memories (3 recent that were two weeks old at time of interview (three weeks old at the time of scanning) - mean 13.3 (SD 2.7) days old; 3 remote that were 10 years old - mean 10.4 (SD 0.57) years old).

Participants recalled each memory fourteen times in a pseudo-random order, while ensuring that the same memory was not repeated twice or more in a row. On each trial, a verbal cue specified which of the six memories a participant should recall. Following this, an instruction appeared on the screen indicating that participants should close their eyes and vividly recall the cued memory. After 12 seconds, an auditory tone signalled them to open their eyes. The participant was then required to provide ratings about the preceding recall trial. First, they rated how vivid the memory was in the preceding recall trial (on a scale of 1 – 5, where 1 was not vivid at all, and 5 was very vivid). Second, they rated how consistently they had

recalled it relative to the unfolding of the event as it occurred originally (where 1 was not consistent at all, and 5 was very consistent). These ratings were used to select only the most vivid and most consistently recalled (i.e. ratings of 4 or 5) memories for inclusion in the MVPA analyses, ensuring that we captured genuine re-experiencing. When trials that were not sufficiently vivid or consistent were excluded, this resulted in an average of 11.58 (SD 0.30) trials for each of the three recent memories and an average of 10.14 (SD 0.89) for each of the three remote memories, with a mean of 63 (33 recent and 30 remote) trials in total per participant that were entered into the MVPA analysis. After scanning, participants rated on a five point scale the effort required to recall the memories, where 1 was very easy to recall, and 5 was very difficult to recall. Both recent (mean 1.25, SD 0.32) and remote (1.58, SD 0.54) memories were recalled with ease. They were also asked “Do you feel that repeatedly recalling a memory changed the memory in any way?”, where 1 was not at all, and 5 was very much. Participants indicated that the memories were hardly changed by multiple repetitions (2.08, SD 0.79).

fMRI data were preprocessed using SPM8 (<http://www.fil.ion.ucl.ac.uk/spm>). We then used a standard MVPA procedure that has been described elsewhere (Chadwick et al., 2010; Bonnici et al., 2012a,b,c) involving a three-way linear support vector machine (SVM) classifier with ten-fold cross-validation (see Supporting Online Material for details). A classifier was created for each subfield in each hemisphere. Results for the left and right hemispheres were highly similar, and therefore the data we report here are collapsed across hemispheres. Each classifier was trained on a portion of the fMRI data relating to the three recent autobiographical memories and then tested on an independent set of instances of these memories. This was also the procedure for remote autobiographical memories. This resulted in two accuracy results for each subfield, one for the recent autobiographical memories and one for the remote autobiographical memories.

We first examined whether it was possible to discriminate between the three recent autobiographical memories from the activity across voxels in each the four subfields. If information was present in the patterns of fMRI activity that enabled discrimination between the three recent memories, then the classifier would produce a classification result significantly above chance (33%). We found that information was present in CA1 and subiculum which permitted successful detection of the three recent autobiographical memories significantly above chance (CA1: $t(11)=3.031$, $p=0.011$; subiculum: $t(11)=2.600$,

$p=0.025$; Fig. 2, blue line). This was not the case for CA3 ($t(11)=1.513$, $p=0.158$) or DG ($t(11)=1.663$, $p=0.125$), where the classifiers' performance was not significantly different from chance. We then examined the remote memories. In contrast to the recent, we found that the three remote autobiographical memories could be detected significantly above chance in all four subfields (CA1: $t(11)=3.786$, $p=0.003$; CA3: $t(11)=3.773$, $p=0.003$; DG: $t(11)=3.372$, $p=0.006$; subiculum: $t(11)=4.227$, $p=0.001$; Fig. 2, red line).

To directly compare recent and remote autobiographical memories, we performed a repeated measures ANOVA. We found a strong trend for the main effect of memory type ($F(1,11) = 4.211$; $p=0.065$) and a significant interaction between subfield and memory type ($F(3,33)=3.092$; $p=0.04$). Post-hoc t-tests revealed that remote autobiographical memories were more readily detected than recent memories in CA3 ($t(11)= -2.257$, $p=0.045$; Fig. 2). A similar trend was also observed in DG ($t(11)= -2.009$, $p=0.07$). No significant differences in classifier performance for recent and remote autobiographical memories were apparent for CA1 ($t(11)= -0.845$, $p=0.416$) or subiculum ($t(11)= -1.267$, $p=0.231$). To summarise, we found that it was possible to detect representations of autobiographical memories in individual hippocampal subfields. Moreover, while CA1 and subiculum contained decodable information about both recent and remote autobiographical memories, information about remote more so than recent memories was detectable in CA3 (with a similar trend in DG).

We then divided the hippocampus into anterior and posterior portions based on the protocol of Hackert et al. 2002 (see also Bonnici et al., 2012a), where the anterior 35% of the hippocampus was labelled as anterior and the remainder as posterior (see Supporting Online Material for mean voxel numbers of each subfield). The end of the uncus was used to delineate the border between the two. MVPA was performed once again, this time on the subfields in the anterior portion (for recent and remote memories), and on the subfields in the posterior portion. There were no significant effects of memory type or subfield in the anterior hippocampal portion (all $F < 1.99$, $p < 0.285$). By contrast, for the posterior portion there was a significant effect of memory type ($F(1,11)=7.635$, $p=0.018$) and a significant subfield by memory type interaction ($F(3,33)=2.9$, $p=0.049$). Post-hoc investigations revealed that remote autobiographical memories were significantly more detectable than recent memories in CA3 and DG (CA3: $t(11)= -4.041$, $p=0.002$; DG: $t(11)= -2.332$, $p=0.040$; CA1: $t(11)= -1.529$, $p=0.155$; subiculum: $t(11)= -1.491$, $p=0.164$; Fig. 3).

To summarise, this analysis shows that while all subfields (CA1, CA3, DG and subiculum) in the anterior hippocampus contained information about both recent and remote autobiographical memories, posterior CA3 and DG only contained decodable information about remote memories. Therefore, while Bonnici et al. (2012a) reported that the hippocampus seems to respect the difference between recent and remote autobiographical memories, our results extend this observation by now showing that it was in particular CA3 and DG that drove this distinction, specifically the portions of these subfields located in the posterior hippocampus. These results therefore resonate with theories that suggest a role for the hippocampus when vividly recollecting autobiographical memories regardless of age (Nadel and Moscovitch, 1997; Winocur and Moscovitch, 2011; Hassabis and Maguire, 2007, 2009).

Perhaps these intra-hippocampal distinctions simply reflect qualitative differences between the recent and remote memories. However, the two memory types were highly similar on a range of characteristics that included vividness, ease of recall, and amount of detail (see Supporting Online Material, Table S1, and Bonnici et al., 2012a for full details of memory matching). Both types of memories were vividly re-experienced suggesting that the remote memories were not more semanticized than the recent memories. Similarly, other factors such as re-encoding, reactivation or the recall of the pre-scan interview, which would have affected both recent and remote memories, cannot easily explain the selective findings for remote memories in specifically posterior CA3 and DG.

Considering reasons for our findings, we need to take into account both the posterior hippocampal location of the differential effect for remote memories, and also the selective involvement of CA3 and DG. The posterior hippocampus has been associated with spatial processing (e.g. Moser and Moser, 1998; Maguire et al., 2000). Bonnici et al. (2012a) suggested that the posterior hippocampus may implement the spatial framework for scenes into which the elements of a memory are re-constructed (Hassabis and Maguire, 2007, 2009), in line with findings from patients with hippocampal damage who have lost the ability to construct spatially coherent scenes (e.g. Hassabis et al., 2007; Race et al., 2011; Mullally et al., 2012 – but see Squire et al., 2010, and Maguire and Hassabis, 2011 for a response). Bonnici et al. (2012a) further speculated that recent memories may be experienced as coherent scenes or events that are temporarily represented in the hippocampus (utilising anterior and posterior aspects), with neocortical consolidation happening relatively quickly.

The constituent elements of autobiographical memories are then the preserve of the neocortex. At retrieval, this piecemeal information is automatically funnelled back into the hippocampus, but in order to be assembled into a coherent form, this requires the scene construction process that takes place in the posterior hippocampus. They suggest this is why remote memories were discernible to a greater degree in posterior hippocampus, because they rely on this process more than do recent memories.

By contrast, CA3 and DG are linked with pattern separation and CA3 with pattern completion (Marr, 1971; Treves and Rolls, 1994; McClelland et al., 1995; Kesner et al., 2004; Leutgeb et al., 2004; Leutgeb et al., 2007; Leutgeb and Leutgeb, 2007; Alvernhé et al., 2008; Hunsaker and Kesner, 2008; Gilbert and Brushfield, 2009; Aimone et al., 2011; O'Reilly et al., 2011). We hypothesise that if remote autobiographical memories have to undergo more reconstruction than recent memories, then the accumulation of memory elements and spatial contexts in posterior hippocampus might trigger CA3-mediated pattern completion to a greater extent. Clearly this is speculative, and additional studies are required to explore this further, as well as to establish precisely what each of the subfields do, both anteriorly and posteriorly, and the functional connectivity between them. The high resolution structural and functional fMRI approach adopted here, and the ability to separate the hippocampal subfields, demonstrates that these kinds of questions are now tractable, presenting new opportunities to examine how autobiographical memories are processed and represented at this fundamental level.

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FIGURE 1. Subfield segmentation. (A) In the coronal plane - coronal sections through an averaged T2-weighted image of the left and right hippocampus of an example participant. (B) Subfield segmentation in the sagittal plane. (C) An example of subfield segmentation in 3D.

FIGURE 2. MVPA results for recent and remote autobiographical memories. Recent and remote memories were represented similarly in CA1 and subiculum. Only remote autobiographical memories were detected significantly above chance in CA3 (* $p < 0.05$), with a similar trend (*) in DG. Error bars represent +/- 1 standard error of the mean; chance=33%.

FIGURE 3. MVPA results for (A) the anterior and (B) the posterior portions of the hippocampus. There were no significant differences in classifier accuracies between recent and remote autobiographical memories in any subfield in the anterior portion. By contrast, two of the subregions within the posterior hippocampus, CA3 and DG, only remote autobiographical memories were detected significantly above chance (* $p < 0.05$). Error bars represent +/- 1 standard error of the mean; chance=33%.

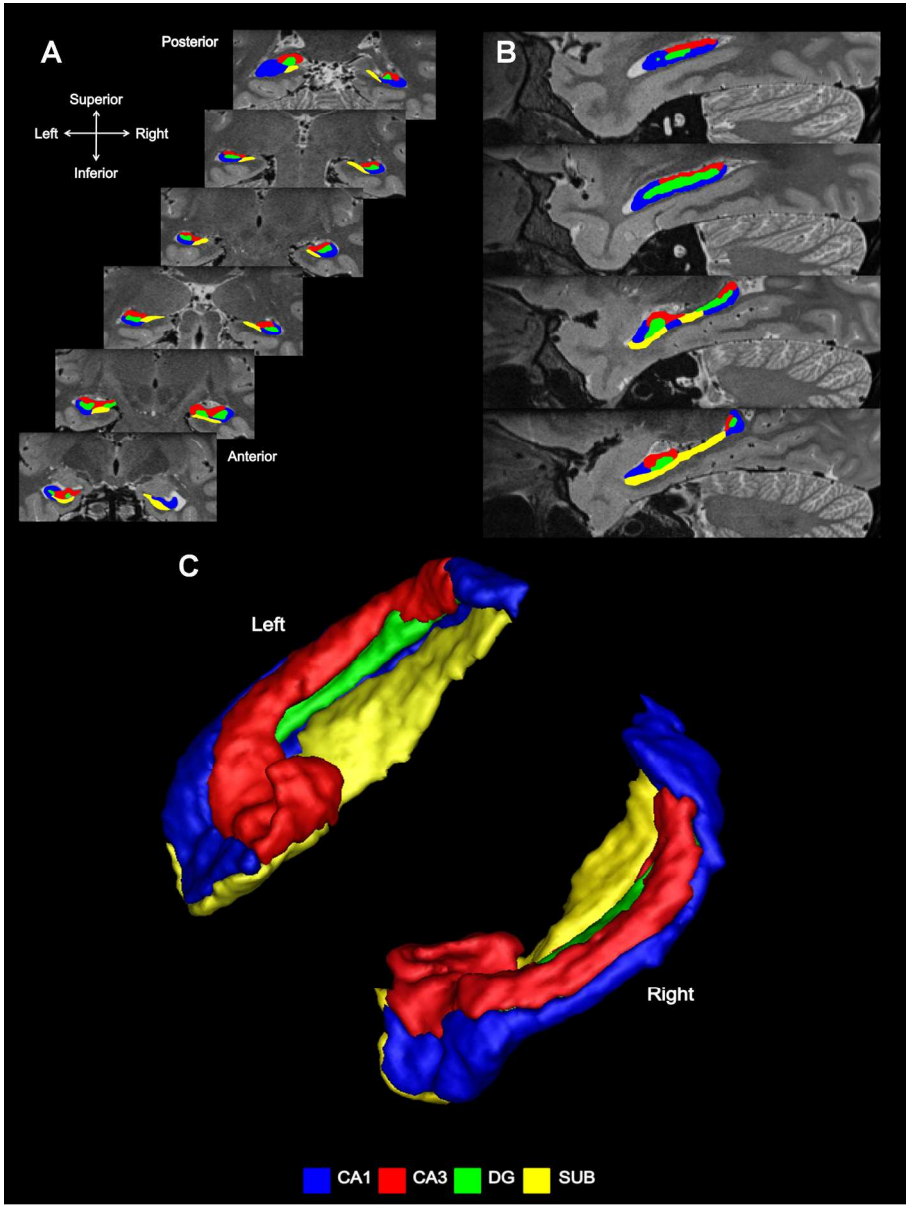


Figure 1
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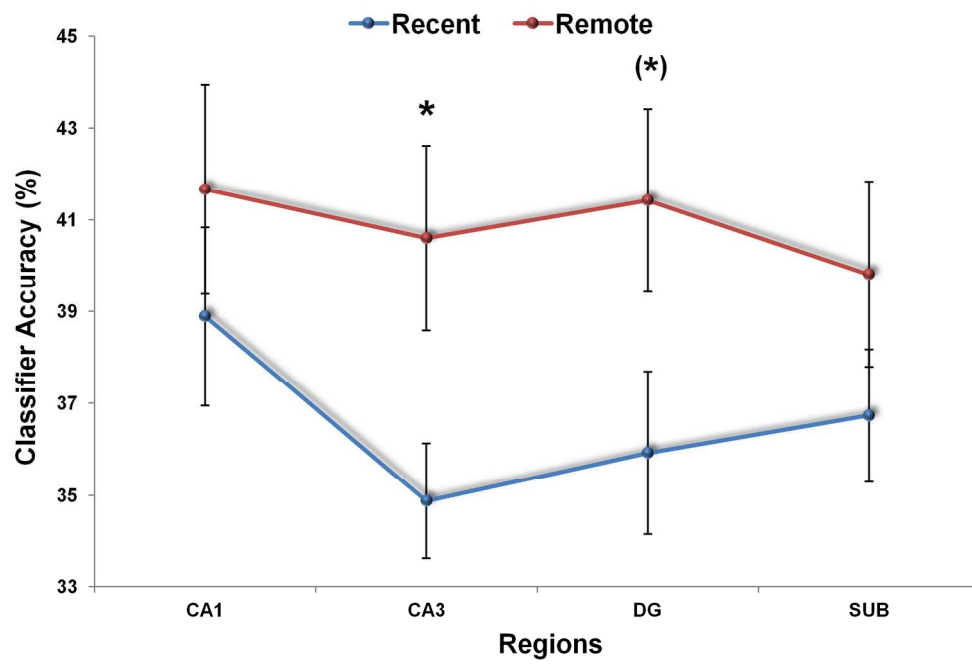


Figure 2
123x82mm (600 x 600 DPI)

Accepte

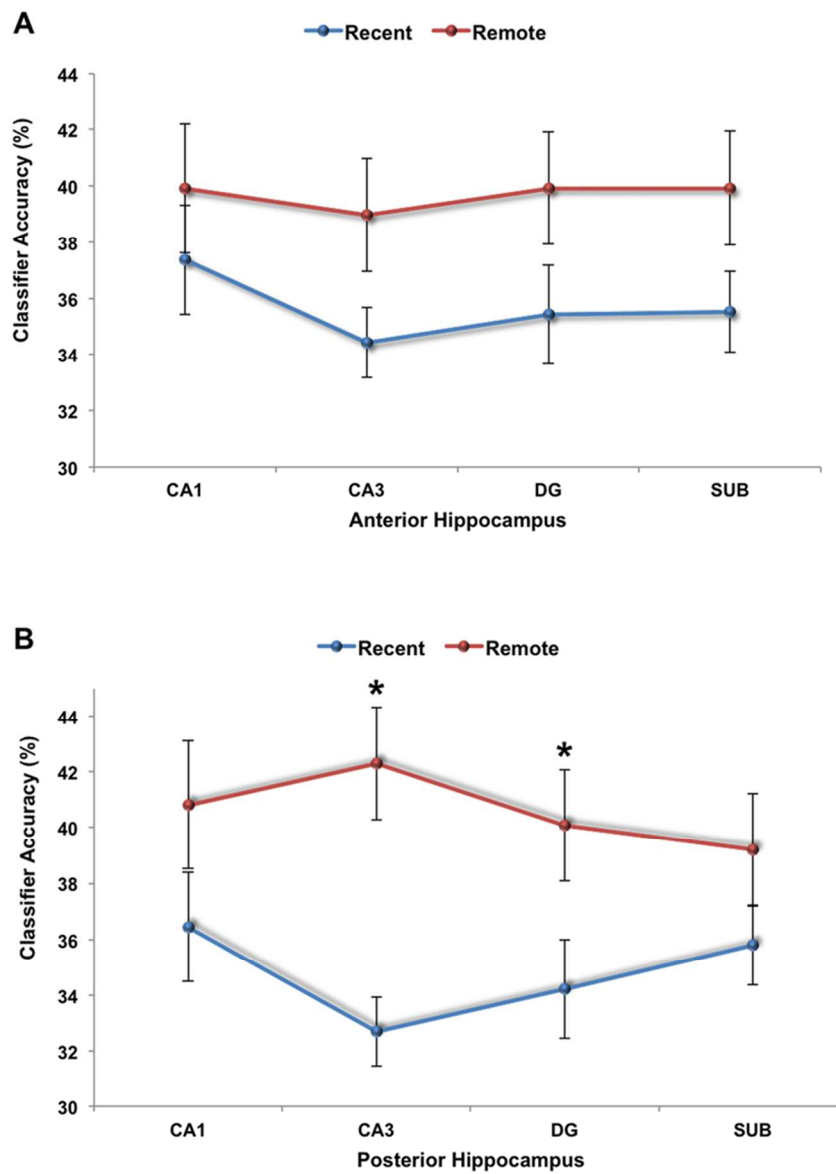


Figure 3
76x104mm (300 x 300 DPI)

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Representations of recent and remote autobiographical memories in hippocampal subfields

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Supporting Online Material

Materials and Methods

The methodological details of this study are described in full in Bonnici et al. (2012a). Key details are reprised here for convenience.

Pre-scan interview

The interview technique employed in this experiment was a standard method used in numerous previous studies (e.g. Maguire et al., 2001; Addis et al., 2004a,b; Summerfield et al., 2009). One week prior to scanning, participants were asked to recollect events that happened from a particular time frame (two weeks ago or ten years ago). An example of the type of memory that was required was provided and it was emphasised that very private or emotional memories, events that happened repeatedly or were very similar to other events, or memories related to public events were not suitable. The memories should unfold in an event-like way, and be very clear and vivid such that when recollecting the memory they felt as if they were re-experiencing the event. Participants were also instructed that they should provide memories that they had rarely thought about since the time the original event had occurred. General probes were given by the interviewer when required (e.g. 'what else can you tell me about this event'). Notes were taken about each memory by the interviewer. Having described a memory, participants then rated each memory along a range of parameters (see Table S1).

Table S1: Memory characteristics

Variable	Recent mean (SD)	Remote mean (SD)	Recent vs Remote t value	p value
Recall frequency before the interview	1.64 (0.611)	1.83 (0.415)	1.258	0.235
Recall frequency between the interview and scan	1.08 (0.208)	1.03 (0.095)	1.483	0.166
Vividness	4.58 (0.352)	4.39 (0.372)	1.549	0.15
Level of detail	4.47 (0.414)	4.14 (0.576)	1.7	0.117
1st/3rd person perspective	1 (0)	1.08 (0.149)	1.915	0.082
Emotional valence	3.17 (0.301)	3.14 (0.172)	0.372	0.717
Active/static event	1 (0)	1.03 (0.095)	1	0.339
Consistency of recall trial-to-trial	4.83 (0.225)	4.72 (0.372)	1.317	0.215

Ratings were on a scale of 1 to 5, where 1 was the minimum and 5 the maximum. For emotional valence: 1,2 = negative, 3 = neutral, 4,5 = positive. For 1st/3rd person perspective: 1 = 1st person, 2 = 3rd person. For active/static event: 1 = active, 2 = static.

During the interview, participants generally recalled 6 to 7 memories from each time period. Based on the ratings for these memories, six memories (three recent and three remote) were then selected from this memory pool to be used in the scan experiment. Several criteria guided the selection of the memories for inclusion. Only those memories that had very high ratings for variables such as vividness (see Table 1), and that were matched to each other both within the recent and remote sets and between the two sets across all the variables, were included. In addition, the experienced interviewer had to be satisfied that the memories were richly detailed and vivid, and seemed to be genuinely re-experienced by the participant. The recent memories were on average 13.3 (SD 2.7) days old, while the remote memories were on average 10.4 (SD 0.57) years old (note that memories were seven days older when scanned a week later). Mean ratings for these memories are shown on Table 1, and confirm that the memories were vivid and could be recalled consistently on repeated occasions. Of note, the memories were also rated as not having been recalled very much since the initial occurrence of the event. Statistical comparisons (two tailed t-tests) between recent and remote memories (also reported on Table 1) showed there were no significant differences between the two types of memory for any of the variables.

The interview material was subjected to a careful review to look for clues that might betray differences between the recent and remote memories used in the scanning experiment, but nothing was found. For instance, we conducted a separate behavioural experiment where 27 naive participants were given the memory cues from the study and were asked to decide whether a memory was recent or remote based on the cues. An ANOVA comparing the

actual memory labels with the participants' labels showed no significant differences, $F(1,69)=2.33$; $p=0.13$). In addition, the memories were coded for the number of overlapping events, locations and people, in case any biases were present: means for recent memories - events: 0; locations: 0; people: 0.4; means for remote memories - events: 0; locations: 0; people: 0.5. It is clear that the amount of inter-memory similarity was very low, and did not differ between the recent and remote memories.

MRI scanning

We acquired high resolution fMRI data in a limited volume focused on the medial temporal lobes, using a 3T Magnetom Allegra head only MRI scanner (Siemens Healthcare, Erlangen, Germany) operated with the standard transmit-receive head coil and a T2*-weighted single-shot echo-planar imaging (EPI) sequence in a single session (in-plane resolution = 1.5×1.5 mm²; matrix = 128×128 ; field of view = 192×192 mm²; 35 slices acquired in interleaved order; slice thickness = 1.5mm with no gap between slices; echo time TE = 30ms; asymmetric echo shifted forward by 26 phase-encoding (PE) lines; echo spacing = 560 μ s; repetition time TR = 3.5s; flip angle $\alpha = 90^\circ$). All data were acquired at 0° angle in the anterior-posterior axis. An isotropic voxel size of $1.5 \times 1.5 \times 1.5$ mm was chosen for an optimal trade-off between BOLD sensitivity and spatial resolution. Further, the isotropic voxel dimension reduced re-sampling artefacts when applying motion correction. To ensure optimal data quality, images were reconstructed online and underwent online quality assurance (Weiskopf et al., 2007). For distortion correction (Hutton et al., 2002), field maps were acquired with the standard manufacturer's double echo gradient echo field map sequence (TE = 10.0 and 12.46 ms, TR 1020ms; matrix size, 64×64), using 64 slices covering the whole head (voxel size $3 \times 3 \times 3$ mm). In addition to the functional scans, a whole brain T1-weighted 3D FLASH sequence was acquired with a resolution of $1 \times 1 \times 1$ mm.

High-resolution structural images were acquired in a limited volume focused on the medial temporal lobes on a 3T whole body MRI scanner (Magnetom TIM Trio, Siemens Healthcare, Erlangen, Germany) operated with the standard transmit body coil and 32-channel head receive coil. A single-slab 3D T2-weighted turbo spin echo sequence with variable flip angles (SPACE, Mugler et al., 2000) in combination with parallel imaging was employed to simultaneously achieve a high image resolution of ~ 500 μ m, high sampling efficiency and short scan time while maintaining a sufficient signal-to-noise ratio (SNR). After excitation of a single axial slab the image was read out with the following parameters: resolution = $0.52 \times$

0.52 x 0.5 mm³, matrix = 384 x 328, partitions = 104, partition thickness = 0.5 mm, partition oversampling = 15.4%, field of view = 200 x 171 mm², TE = 353 ms, TR = 3200 ms, GRAPPA x 2 in phase-encoding (PE) direction, bandwidth = 434 Hz/pixel, echo spacing = 4.98 ms, turbo factor in PE direction = 177, echo train duration = 881, averages = 1.9. For reduction of signal bias due to, for example, spatial variation in coil sensitivity profiles, the images were normalized using a prescan and a weak intensity filter was applied as implemented by the scanner's manufacturer. To improve the SNR of the anatomical image, four scans were acquired for each participant, coregistered and averaged.

Delineating the hippocampal subfields

Manual segmentation of the subfields was performed using the protocol of Bonnici et al. (2012b) on the averaged T2 high-resolution (0.5mm³) structural images of each participant. This resulted in identification of CA1, CA3, DG and subiculum for each participant in each hemisphere. The average amount of time taken to segment the subfields of one hippocampus was approximately two days. Intra-rater reliability was calculated using the Dice overlap metric (Dice, 1945), defined as the volume of overlap between two regions of interest, divided by the mean volume. As in other subfield segmentation studies (Van Leemput et al., 2008; Yushkevich et al., 2009; Malykhin et al., 2010), five consecutive slices located in the body of the hippocampus were chosen. Intra-rater reliability was assessed by comparing two sets of segmentations performed by HMB with a 6 month interval between segmentations: CA1 0.80, CA3 0.77, DG 0.74, subiculum 0.82. The mean number of (1.5mm³) voxels in each subfield was: *whole hippocampus* – CA1 493.38 (68.76), CA3 299.04 (32.47), DG 201.67 (21.58), subiculum 227.38 (32.97); *anterior portion* – CA1 232.88 (42.38), CA3 158.38 (24.85), DG 125.33 (16.05), subiculum 93.42 (19.10); *posterior portion* – CA1 308.29 (34.49), CA3 158.21 (25.45), DG 139.38 (19.57), subiculum 139.04 (24.98).

Image preprocessing

Image pre-processing was performed using SPM8 (<http://www.fil.ion.ucl.ac.uk/spm>). The first six EPI volumes were discarded to allow for T1 equilibration effects (Frackowiak et al., 2004). The remaining EPI images were then realigned to correct for motion effects, and minimally smoothed with a 3mm FWHM Gaussian kernel. A linear detrend was run on the images to remove any noise due to scanner drift (LaConte et al., 2005) using customised matlab code. Next the data were convolved with the canonical hemodynamic response function (HRF) to increase the signal-to-noise ratio (Frackowiak et al., 2004). This HRF

convolution effectively doubled the natural BOLD signal delay, giving a total delay of approximately 12s. To compensate for this delay, all onset times were shifted forward in time by three volumes, yielding the best approximation to the 12s delay given a TR of 3.5s and rounding to the nearest volume. Analysis focused on the 12 second periods of vivid recall giving a total of four functional volumes per trial.

MVPA

Overview: A support vector machine (SVM) classifier was created for each subfield. Each classifier was trained on a portion of the fMRI data relating to the three recent memories and then tested on an independent set of instances of these memories. This was also the procedure for remote memories. This resulted in two accuracy results for each subfield, one for the recent memories and one for the remote memories.

Procedure: We used a standard MVPA procedure that has been described in detail elsewhere (Chadwick et al., 2010, 2012; Bonnici et al., 2012a,b,c). To reprise briefly, the overall classification procedure involved splitting the fMRI data into two segments: a “training” set used to train a classifier with fixed regularization hyperparameter $C = 1$, in order to identify response patterns related to the memories being discriminated, and a “test” set used to independently test the classification performance (Duda et al., 2001), using a ten-fold cross-validation procedure. Prior to multivariate classification, feature selection (Guyon and Elisseeff, 2003) was performed on the data from the training set (thereby ensuring that this step was fully independent from final classification, which is critical for avoiding “double-dipping”, Kriegeskorte et al., 2009). This was conducted using a standard multivariate searchlight strategy within a region of interest. For a given voxel, we first defined a small sphere with a radius of three voxels centred on the given voxel (Kriegeskorte et al., 2006; see also Hassabis et al., 2009; Chadwick et al., 2010, 2012; Bonnici et al., 2012a,c). Note that the spheres were restricted so that only voxels falling within the given region of interest were included. Therefore, the shape of the sphere and the number of voxels within it varied depending on the proximity to the region of interest’s borders. This procedure then allowed the selection of the searchlight voxel set that contained the greatest degree of decoding information within the training dataset. Using this voxel subset, the SVM classifier was trained to discriminate between, for example, the three recent memories using the “training” image dataset, and tested on the completely independent “test”

dataset. The classification was performed using the LIBSVM implementation (Chang and Lin, 2011).

Standard SVMs are binary classifiers that operate on two-class discrimination problems, whereas our data involved a three-class problem (i.e. three recent memories or three remote memories). The SVM can, however, be arbitrarily extended to work in cases where there are more than two classes. Typically this is done by reducing the single multiclass problem into multiple binary classification problems that can be solved separately and then recombined to provide the final class prediction (Allwein et al., 2000). We used the well-established Error Correcting Output Codes approach (Dietterich and Bakiri, 1994) and computing of the Hamming distance (Hamming, 1950) as described in detail elsewhere (Hassabis et al., 2009; Chadwick et al., 2010).

Data analysis

The classifier accuracy values for each subfield were compared to chance. Given that we were only interested in whether results were significantly above chance, one tailed t-tests were used. Other comparisons were conducted using repeated measures ANOVAs and significant results were subsequently interrogated using two-tailed paired t-tests. A threshold of $p < 0.05$ was employed throughout.

Results

In another set of analyses, we collapsed across individual memories and examined whether it was possible to in general distinguish recent from remote memories. Table S2 below summarises the results, for each entire subfield ('whole'), and the anterior ('ant') and posterior ('post') segments of each subfield. In line with previous findings reported by Bonnici et al. (2012a), we found that classifiers operating in each hippocampal subregion could classify recent and remote autobiographical memories significantly above chance (which was 50%).

Table S2: Recent versus remote memory decoding

Region	t-value	df	sig(2-tailed)	sig(1-tailed)
CA1whole	3.396	11	.006	.003
CA3whole	3.120	11	.010	.005
DGwhole	3.906	11	.002	.001
SUBwhole	3.229	11	.008	.004
CA1ant	4.017	11	.002	.001
CA3ant	4.029	11	.002	.001
DGant	3.301	11	.007	.004
SUBant	3.005	11	.012	.001
CA1post	2.465	11	.031	.002
CA3post	2.799	11	.017	.009
DGpost	2.648	11	.023	.011
SUBpost	2.859	11	.016	.008

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