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Non-monotonic recruitment of ventromedial prefrontal cortex during remote memory recall

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Short title: vmPFC and remote memory

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Abstract

Systems-level consolidation refers to the time-dependent reorganisation of memory traces in the neocortex, a process in which the ventromedial prefrontal cortex (vmPFC) has been implicated. Capturing the precise temporal evolution of this crucial process in humans has long proved elusive. Here, we used multivariate methods and a longitudinal functional MRI design to detect, with high granularity, the extent to which autobiographical memories of different ages were represented in vmPFC and how this changed over time. We observed an unexpected time-course of vmPFC recruitment during retrieval, rising and falling around an initial peak of 8-12 months, before re-engaging for older two and five year old memories. This pattern was replicated in two independent sets of memories. Moreover, it was further replicated in a follow-up study eight months later with the same participants and memories, where the individual memory representations had undergone their hypothesised strengthening or weakening over time. We conclude that the temporal engagement of vmPFC in memory retrieval seems to be non-monotonic, revealing a complex relationship between systems-level consolidation and prefrontal cortex recruitment that is unaccounted for by current theories.

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Author Summary

Our past experiences are captured in autobiographical memories which allow us to recollect events from our lives long after they originally occurred. A part of the brain's frontal lobe, called the ventromedial prefrontal cortex or vmPFC, is known to be important for supporting autobiographical memories especially as memories become more remote. The precise temporal profile of the vmPFC's involvement is unclear, yet this information is vital if we are to understand how memories change over time and the mechanisms involved. In this study we sought to establish the time-course of vmPFC engagement in the recollection of autobiographical memories while participants recalled memories of different ages during functional magnetic resonance imaging (fMRI). Using a method that detects brain activity patterns associated with individual memories, we found that memory-specific neural patterns in vmPFC became more distinct over the first few months after a memory was formed, but then this initial involvement of vmPFC subsided after one year. However, more remote memories (two years and older), appeared to re-engage vmPFC once again. This temporal profile is difficult to accommodate within any single existing theory. Consequently, our results provoke a re-think about how memories evolve over time and the role played by the vmPFC.

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Introduction

We possess a remarkable ability to retrieve, with ease, one single experience from a lifetime of memories. How these individual autobiographical memories are represented in the brain over time is a central question of memory neuroscience which remains unanswered.

Consolidation takes place on two levels which differ on both a spatial and temporal scale. On a cellular level, the stabilisation of new memory traces through modification of synaptic connectivity takes only a few hours [1], and is heavily dependent upon the hippocampus [2-5]. On a much longer timescale, the neocortex integrates new memories, a form of consolidation termed "systems-level" [6]. The precise timeframe of this process is unknown. A related long-standing debate which has contributed to this uncertainty is whether or not the hippocampus ever relinquishes its role in autobiographical memory retrieval. One theory asserts that the hippocampus is not involved in the retrieval of memories after they have become fully consolidated to the neocortex [7]. Alternate views maintain that vivid, detailed autobiographical memories retain a permanent reliance on the hippocampus for their expression [8-12].

An undisputed feature of systems-level consolidation, however, is the strengthening of neural representations in the neocortex over time. Clarity on the time course of systems-level consolidation is therefore more likely to be achieved through scrutiny of its neocortical targets. While theoretical accounts often fail to specify these cortical locations, animal experiments have consistently implicated the medial prefrontal cortex. While this region has been associated with the formation [13, 14] and recall of recently acquired memories [15-17], in rodents it appears to be disproportionately involved in the retrieval of memories learned weeks previously [18-26]. The dependency on this region, which emerges over time, is facilitated by post-learning activation [27] and structural changes [28-30].

The evolutionary expansion of prefrontal cortex in humans makes it challenging to make direct anatomical comparisons with rodents, but the ventromedial prefrontal cortex (vmPFC) has been proposed as a homologous site of long-term memory consolidation [31]. It may appear surprising that an association between impaired autobiographical memory retrieval and vmPFC lesions has only recently started to be more precisely characterised [32]. However, there are a number of confounding factors in

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this field [33] - non-selectivity of vmPFC lesions, methodological differences in memory elicitation, and the tendency of patients with vmPFC damage to recollect events which have never occurred, a phenomenon known as confabulation [34].

Numerous functional MRI (fMRI) studies of vmPFC activity during autobiographical memory recall have been conducted, but with inconclusive results. Delay-dependent increases in retrieval-related activity have been observed in some studies [35, 36] but not others [37-39]. Autobiographical memory in particular induces robust vmPFC engagement [40] but it is unclear whether this activity increases [41], decreases [42], or remains constant in accordance with memory remoteness [43-52].

A powerful method of fMRI analysis which can help to bridge the empirical gap between the human and animal literatures is multi-voxel pattern analysis (MVPA), due to its increased sensitivity to specific neural representations [53]. Using this approach, Bonnici et al. [54] demonstrated that remote 10 year old autobiographical memories were more detectable in the vmPFC than recent two week old autobiographical memories, consistent with its proposed role as a long-term consolidation site. This difference was not apparent in other cortical areas, nor did it emerge from a standard univariate analysis. A follow up study two years later with the same participants and memories, demonstrated that the original two week old memories were now as detectable in the vmPFC as the remote memories [55]. This suggested the recent memories had been fully consolidated in the vmPFC after just two years, and perhaps even sooner.

The identification of this two year time window represented an opportunity to resolve the time course of systems-level consolidation with high precision. To do so, we sampled memories from four month intervals spanning a two year period, and compared their neural representations using fMRI. As opposed to the pattern classification approach employed by Bonnici et al. [54] to decode the neural signatures of individual memories, we used Representational Similarity Analysis (RSA) [56]. This method compares the consistency of neural patterns across repetitions of a single memory, against all other unrelated memories, to detect its unique informational content in a region of interest. Differences in the strength of memory representations across time periods were interpreted as delay-dependent

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engagement of the vmPFC. To verify observed time-sensitive differences, we followed the neural evolution of individual memories in a follow up study with the same participants and memories eight months later. The selection of numerous time-points characterised the consolidation process with unprecedented temporal resolution, while the longitudinal design was not only an opportunity to replicate these findings, but to observe systems-level consolidation in action.

Systems-level consolidation is generally assumed to be an incremental process, therefore, we considered a gradual linear trajectory of vmPFC recruitment as the most likely outcome. The alternative hypothesis was a rapid strengthening of vmPFC neural representations in the first few months after an event. The results conformed to neither scenario, and revealed an unexpected temporal relationship - a transient recruitment of the vmPFC beginning in the months following the initial experience, followed by an enduring signature of more remote memories. The second, longitudinal, experiment confirmed this finding. This is the first demonstration, to our knowledge, of such a temporal dissociation in vmPFC-mediated memory retrieval.

Results

Experiment 1

One week prior to the fMRI scan, with the assistance of personal photographs, participants (n=30) verbally recalled and rated the characteristics of autobiographical memories from eight time periods: memories that were 0.5 months old (0.5M, i.e., two week old memories), 4M, 8M, 12M, 16M, 20M, 24M and also 60M old – these latter memories serving as a definitive benchmark for remote (5 year old) memories (see Materials and methods, Fig 1A). Two memories from each time period which were sufficiently vivid, detailed, specific and unique in time and place were chosen for subsequent recall in the scanner. This meant that there were two full sets of memories. Participants created a short phrase pertaining to each autobiographical memory, which was paired with the photograph to facilitate recall during the subsequent fMRI scan.

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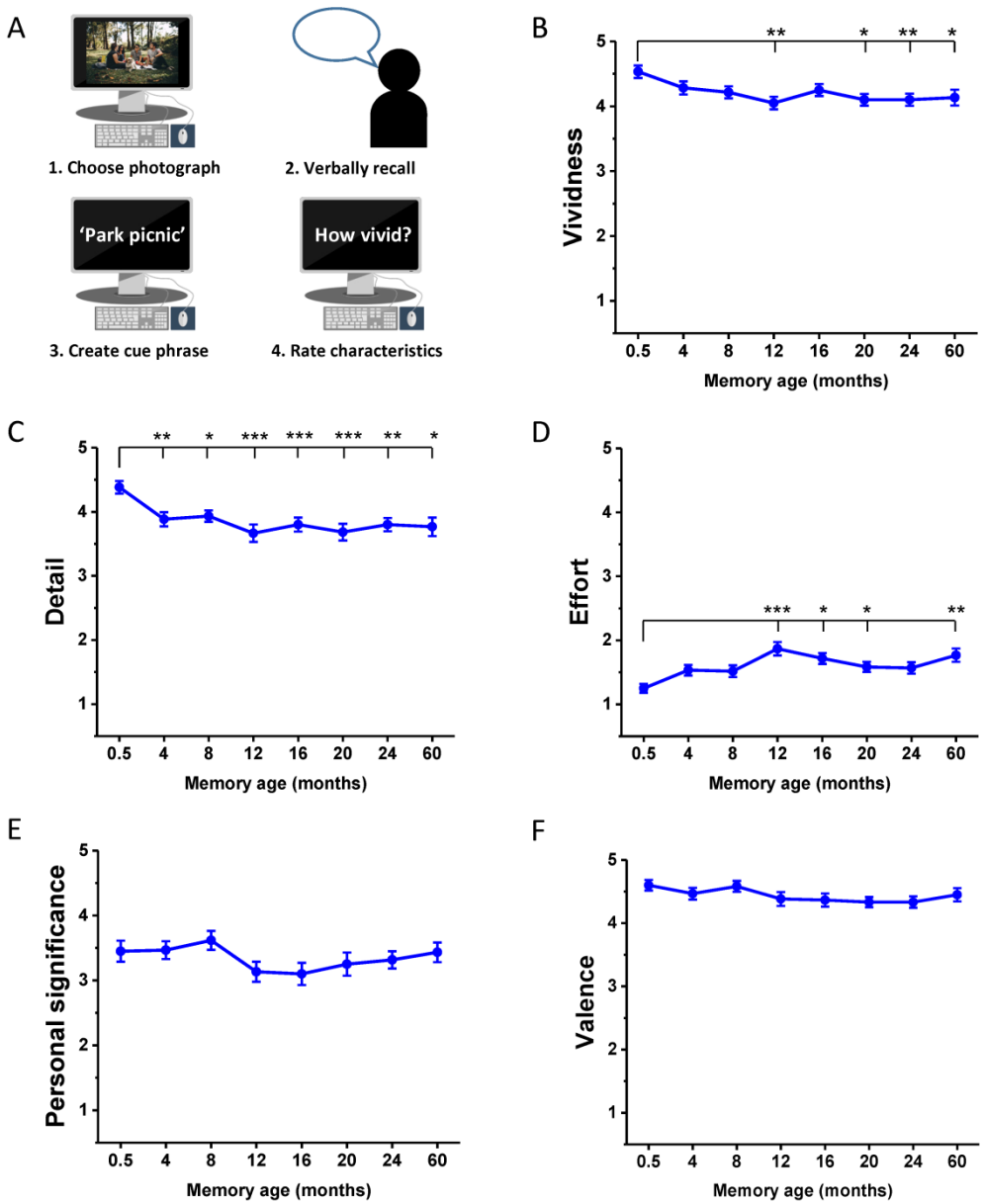

Fig 1. Memory harvesting and subjective ratings. (A) Schematic of the interview where the autobiographical memories were harvested. Participants recalled a memory which was cued by a personal photograph, chose a phrase to help remind them of this memory during the subsequent scanner task, and rated its characteristics. (B-F) Subjective ratings (means +/- 1SEM; see also means and SDs in Table A in S1 Table, and S1 Data for individual ratings across both sets of memories) of memory characteristics at each time period for Experiment 1, averaged across the two sets of memories. Ratings were on a scale of 1 to 5, where 1 was low and 5 was high. For emotional valence: 1-2 = negative, 3 = neutral, 4-5 = positive. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Comparable subjective recall phenomenology across memories

While all memories satisfied the criteria of being vivid and detailed, and the ratings were high (Fig 1; see means and SDs in Table A in S1 Table), subjective vividness nevertheless varied as a function of memory age ($F_{(7,203)} = 3.45$, $p = 0.002$), with the most recent, 0.5M old, memories rated higher than 12M (t_{29} =

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153 4.08, p = 0.009), 20M (t_{29} = 3.88, p = 0.016), 24M (t_{29} = 4.18, p = 0.007) and 60M old memories (t_{29} =
154 3.45, p = 0.049, Fig 1B). Subjective ratings of detail also differed across time-points ($F_{(7,203)}$ = 5.74, p <
155 0.001), once again the most recent 0.5M old memories were rated higher than 4M (t_{29} = 4.45, p = 0.003),
156 8M (t_{29} = 3.97, p = 0.012), 12M (t_{29} = 5.00, p < 0.001), 16M (t_{29} = 4.96, p < 0.001), 20M (t_{29} = 5.37, p <
157 0.001), 24M (t_{29} = 4.51, p = 0.003) and 60M old memories (t_{29} = 3.98, p = 0.012, Fig 1C). The expenditure
158 of effort during recall also varied according to remoteness of memories ($F_{(7,203)}$ = 5.79, p < 0.001), with
159 0.5M old memories being easier to recollect than 12M (t_{29} = -5.29, p < 0.001), 16M (t_{29} = -3.90, p =
160 0.015), 20M (t_{29} = -3.67, p = 0.027) and 60M old memories (t_{29} = -4.55, p = 0.003, Fig 1D). No significant
161 difference was observed across time periods from 4M to 60M on any of these characteristics (all p >
162 0.05), nor did memories differ in their personal significance ($F_{(7,203)}$ = 1.66, p = 0.120, Fig 1E) or emotional
163 valence ($F_{(7,203)}$ = 1.51, p = 0.166, Fig 1F) as a function of age.

164 In addition to these main ratings of interest, no difference was reported in the extent to which
165 memories were recalled as active or static ($F_{(7,203)}$ = 1.36, p = 0.224), or from a first or third person
166 perspective ($F_{(3.69,107.02)}$ = 1.09, p = 0.365) across time periods. The reported frequency at which
167 memories were recalled since the original event (rated on a five point scale from “never” to “very
168 frequently”), differed as a function of time ($F_{(5.11,148.04)}$ = 4.36, p < 0.001), with the most recent 0.5M old
169 memories thought about more frequently than 12M (t_{29} = 4.37 p = 0.004), 16M (t_{29} = 3.47, p = 0.046) and
170 24M (t_{29} = 3.71, p = 0.024) old memories (see S11 Data for individual ratings for these characteristics).

171 Overall, therefore, memories were generally well matched on subjective phenomenological
172 ratings, satisfied the criteria of high quality of memory recall, with only small differences observed for
173 the most recent 0.5M old memories compared to the other autobiographical memories, as might be
174 expected.

175

176 ***Consistent level of details recalled across memories***

177 To complement the subjective ratings of memory characteristics with a more objective assessment of
178 their content, transcripts of participants’ memory interviews were scored using the Autobiographical

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Interview protocol ([57]; Materials and methods). In total for this first experiment, 10,187 details were scored. The mean (SD) number of internal details (bound to the specific 'episodic' spatiotemporal context of the event) and external details (arising from a general 'semantic' knowledge or references to unrelated events) are shown in Table B in S1 Table (see also Fig 2). They were then compared across time periods. In contrast to the subjective ratings of memory detail, the number of details recalled across memories from different time periods displayed only a non-significant trend ($F_{(4.54,131.66)} = 1.92$, $p = 0.101$). As expected, the number of internal and external details differed ($F_{(1,29)} = 206.03$, $p < 0.001$), with more internal details recalled for every time period (all $p < 0.001$). No interaction between time period and type of detail was observed ($F_{(7,203)} = 1.87$, $p = 0.077$). While a more targeted contrast of the most recent (0.5M) and most remote (60M) memories did reveal that 0.5M events contained more internal details ($t(29) = 3.40$, $p = 0.002$), this is consistent with participants' subjective ratings, and implies that any observed strengthening of neural representations over time could not be attributable to greater detail at remote time-points. The number of external details recalled was remarkably consistent across all time periods, emphasising the episodic nature of recalled events irrespective of remoteness. Inter-rater reliabilities for the scoring (see Materials and methods) were high for both internal (ICC = 0.94) and external (ICC = 0.81) details.

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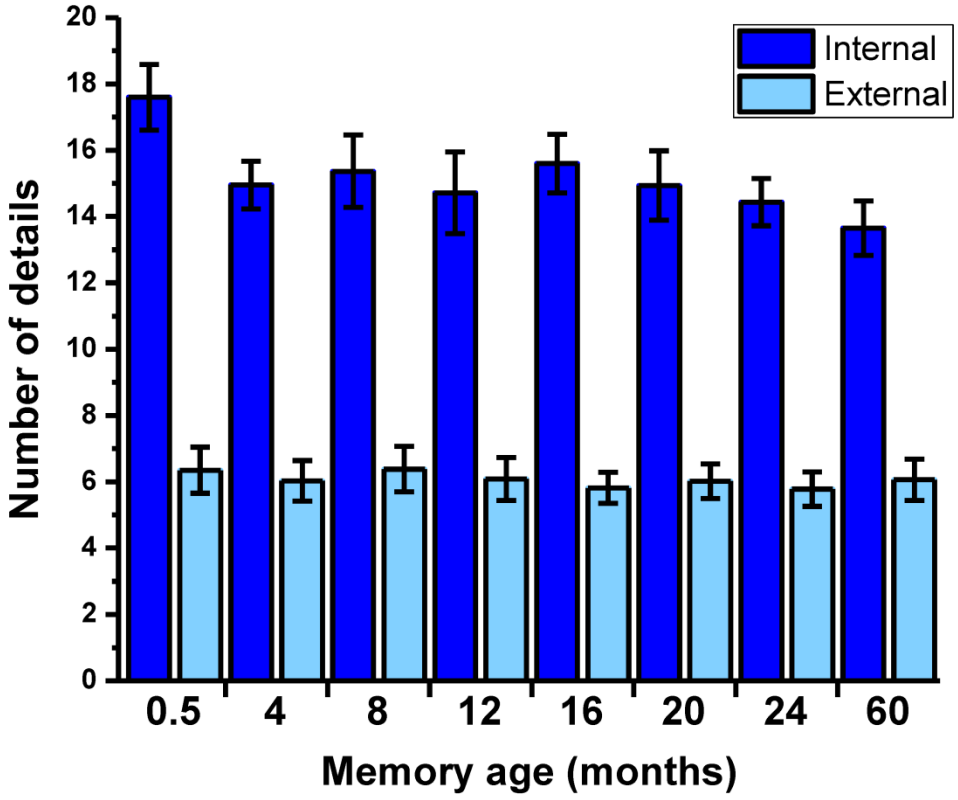

Fig 2. Objective scores for memory details. The mean +/- 1SEM (see also means and SDs in Table B in S1 Table, and S2 Data for individual participant scores) number of internal and external details at each time period, averaged across the two sets of autobiographical memories.

vmPFC engagement during recall was non-monotonic

vmPFC was delineated as the ventral medial surface of the frontal lobe and the medial portion of the orbital frontal cortex [58]. This comprises areas implicated in memory consolidation [31, 54, 55], namely Brodmann Areas 14, 25, ventral parts of 24 and 32, the caudal part of 10 and the medial part of BA 11 (Fig 3A, and Materials and methods).

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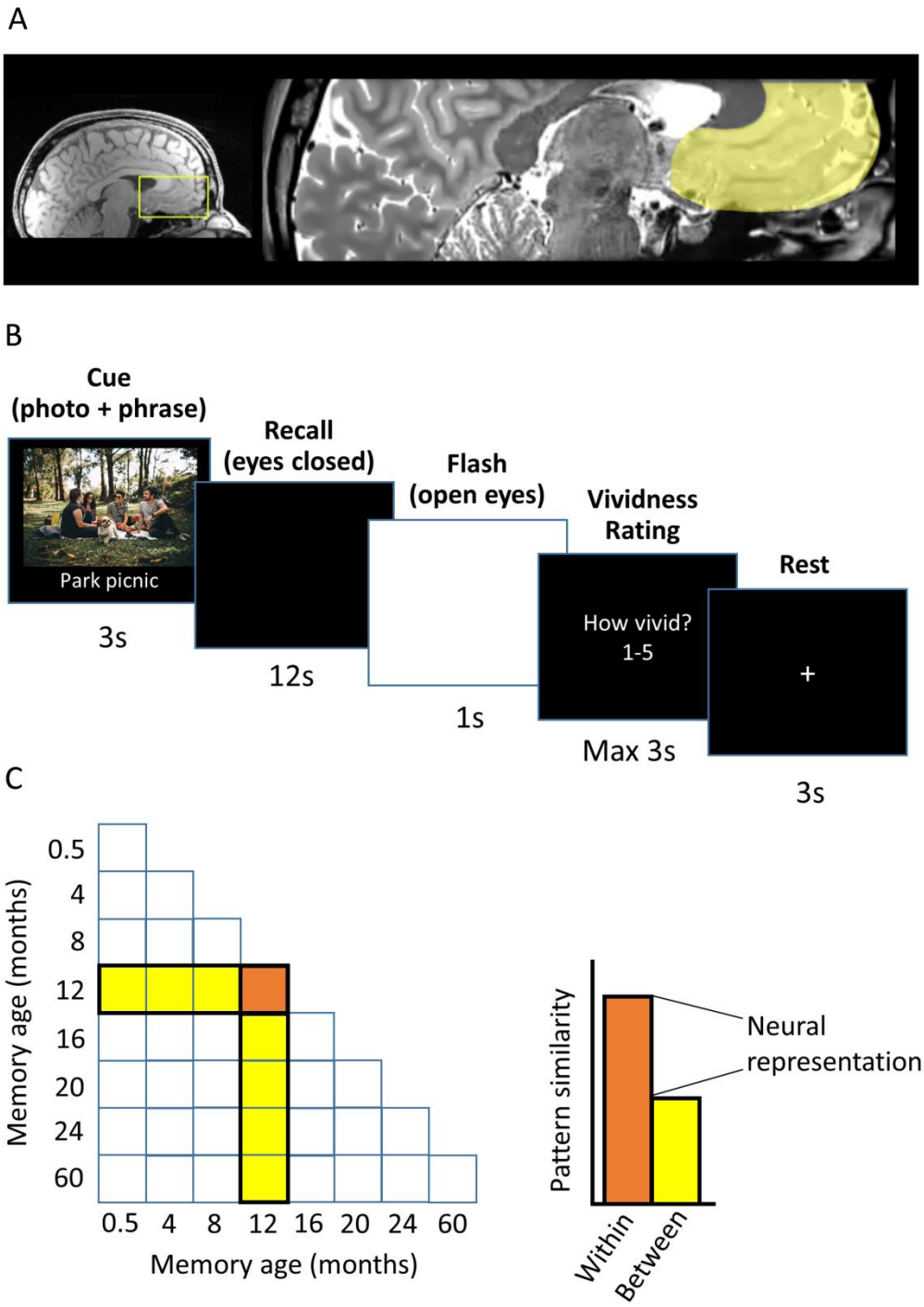

Fig 3. Experimental details. (A) The vmPFC is highlighted on an example participant's structural MRI scan. (B) The timeline of an example trial from the scanning task. (C) Graphical illustration of the neural representation score calculation using RSA. The neural pattern similarity across trials recalling the same memory (orange) minus the mean pattern similarity between that memory and other memories (yellow) generates a "neural representation" score. A score significantly higher than zero indicates a neural pattern distinct to that memory is present in the vmPFC.

On each trial, the photograph and associated pre-selected cue phrase relating to each event were displayed on a screen for 3 seconds. Following removal of this cue, participants then closed their

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218 eyes and recalled the memory. After 12 seconds, the black screen flashed white twice, to cue the
219 participant to open their eyes. The participant was then asked to rate how vivid the memory recall had
220 been using a five-key button box, on a scale of 1-5, where 1 was not vivid at all, and 5 was highly vivid
221 (Fig 3B).

222 We used RSA to quantify the extent to which the strength of memory representations in the
223 vmPFC differed as a function of memory age. This was achieved by contrasting the similarity of neural
224 patterns when recalling the same memory with their similarity to other memories to yield a "neural
225 representation" score for each memory (see Materials and methods, Fig 3C). As there were two
226 memories recalled per time period, the neural representation scores were averaged to produce one
227 value for that time period.

228 We anticipated an increase in the strength of memory representations at some point between
229 0.5M and 24M, in line with the results of Bonnici and Maguire [55]. This is what we observed, where the
230 most recent 0.5M memories were undetectable (t_{29} = 0.72, p = 0.477) in vmPFC, in contrast to the
231 distinct neural signatures observed for 4M (t_{29} = 2.85, p = 0.008), 8M (t_{29} = 3.09, p = 0.004) and 12M (t_{29}
232 = 3.66, p < 0.001) old memories (Fig 4A). These changes in the strength of memory representations were
233 significant across time periods ($F_{(7,203)}$ = 2.22, p = 0.034), with an observed increase in vmPFC recruitment
234 from 0.5M to 8M (t_{29} = 2.07, p = 0.048) and 12M (t_{29} = -2.20, p = 0.036).
235

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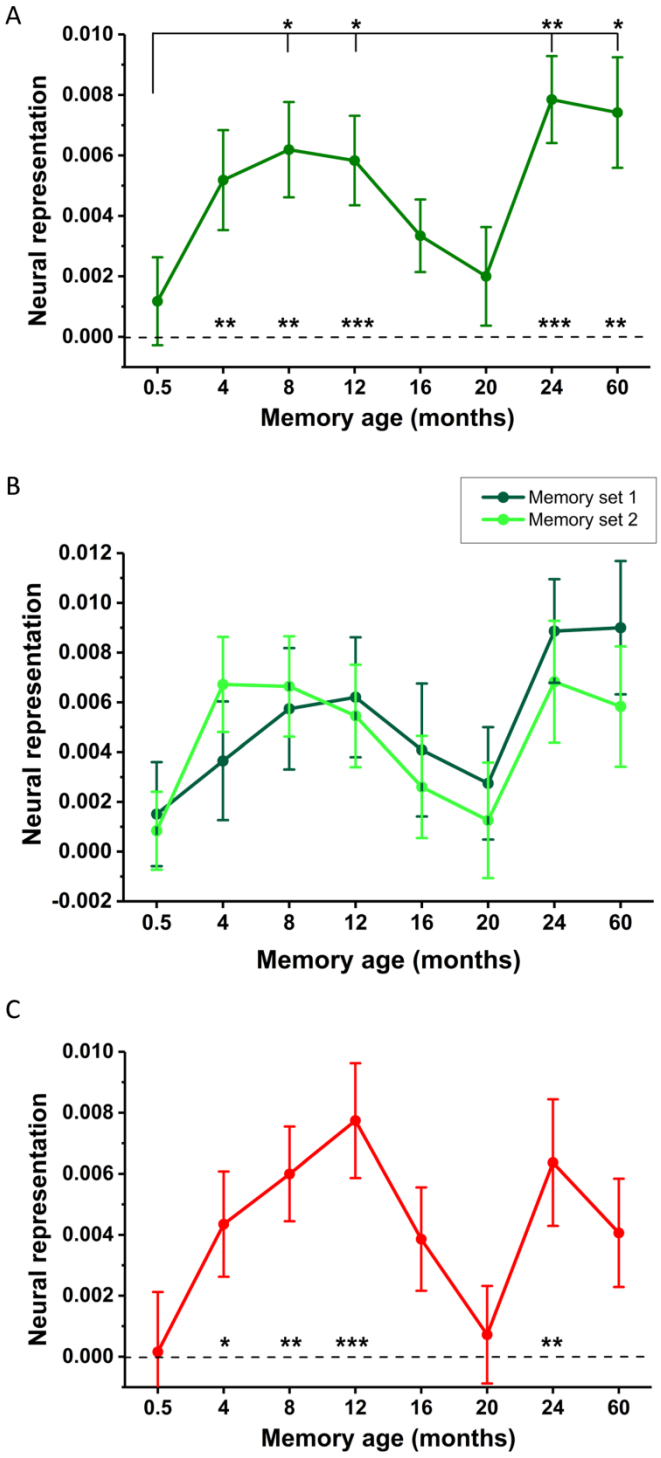

Fig 4. fMRI results of Experiment 1. (A) Mean +/- 1SEM neural representation scores at each time-point averaged across the two sets of memories. Asterisks above the dotted line indicate detectability of memories in vmPFC at each time-point. Asterisks above the solid line indicate significant increases in memory representations compared to the most recent (0.5M old) memories. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. See S1 Fig for the underlying representational similarity matrix and S2 Fig for a boxplot distribution of these data. (B) Neural representation scores at each time-point plotted separately for the two sets of autobiographical memories. (C) Neural representation scores when using a single identically-aged memory as a baseline. See S3 Data for individual participant scores.

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246
247 However, what was observed for the following two time periods was unexpected – an apparent
248 disengagement of the vmPFC over the next eight months as we observed weak detectability of memory
249 representations in vmPFC for 16M (t_{29} = 1.85, p = 0.074) and 20M (t_{29} = 1.03, p = 0.310) old memories.
250 Neither 16M (t_{29} = -1.06, p = 0.298) nor 20M memories (t_{29} = -0.40, p = 0.691) were more strongly
251 represented than the recent 0.5M old memories. In contrast, the more remote 24M (t_{29} = 4.34, p <
252 0.001) and 60M (t_{29} = 3.55, p = 0.001) memories were detectable in the vmPFC, and significantly more so
253 than the most recent memories (24M vs 0.5M, t_{29} = -2.93, p = 0.007; 60M vs 0.5M, t_{29} = -2.54, p = 0.017)
254 as well as the more temporally proximal 20M old memories (24M vs 20M, t_{29} = -2.50, p = 0.018; 60M vs
255 20M, t_{29} = -2.32, p = 0.028).

256 The experimental design afforded us the opportunity to verify this non-monotonic pattern. As
257 we sampled two memories per time-point, this time-dependent pattern should be evident in both sets
258 of memories. As shown in Fig 4B, the two sets of memories followed a similar time-course of changes in
259 representation within vmPFC. This is a compelling replication, given that the two memories from each
260 time-period were unrelated in content as a prerequisite for selection, recalled in separate sessions in the
261 scanner and analysed independently from each other.

262 The availability of two memories at each time-point also permitted the use of an alternative
263 approach to calculating neural representation scores. Instead of using the similarity to memories from
264 other time-points as a baseline, we could also assess if memories were similar to their temporally
265 matched counterpart in the other set. As can be seen in Fig 4C, the non-monotonic pattern is preserved
266 even when just using one identically aged memory as a baseline. In other words, the distinguishable
267 patterns are specific to each individual memory rather than attributable to general retrieval processes
268 associated with any memory of the same age.

269 An alternative explanation for memory representation scores which decreased over time is that
270 the neural patterns became increasingly similar to memories from other time-points, rather than less
271 consistent across repetitions, perhaps again reflecting more general retrieval processes. However as

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evident in S3 Fig, between-memory scores remained stable across all time-points, and did not differ in their statistical significance ($F_{(5.24,152.02)}$ = 1.72, p = 0.13). If anything, there was a slight trend for higher between-memory scores to accompany higher within-memory scores. Therefore, the detectability of neural representations appeared to be driven by consistent within-memory neural patterns.

The observed temporal relationship is unique to vmPFC

Our main focus was the vmPFC, given previous work highlighting specifically this region's role in representing autobiographical memories over time [54, 55]. We also scanned within a partial volume (to attain high spatial resolution with a reasonable TR), so were constrained in what other brain areas were available for testing (see Materials and methods). Nevertheless, we examined the same brain areas as Bonnici et al. [54], Bonnici and Maguire [55], additionally including the precuneus, given its role in autobiographical memory retrieval [59], and in no case did we observe a significant change in memory detectability across time periods - entorhinal/perirhinal cortex ($F_{(7,203)}$ = 1.55, p = 0.154), hippocampus ($F_{(7,203)}$ = 0.98, p = 0.445), posterior parahippocampal cortex ($F_{(7,203)}$ = 1.41 p = 0.202), retrosplenial cortex ($F_{(7,203)}$ = 0.69, p = 0.682), temporal pole ($F_{(7,203)}$ = 1.78, p = 0.093), lateral temporal cortex ($F_{(4.86,141.03)}$ = 0.68, p = 0.636) or precuneus ($F_{(7,203)}$ = 0.789, p = 0.562). Of note, memories which were undetectable in the vmPFC were still represented in other brain regions at these time points (see S2 Table for neural representation score means and SDs, and S13 Data for individual participant scores). For example, 20 month old memories which did not appear to recruit the vmPFC during retrieval were represented in the majority of other regions comprising the core autobiographical memory network (precuneus, lateral temporal cortex, parahippocampal cortex, and approaching significance in the retrosplenial cortex (t_{29} = 1.83, p = 0.08)).

Following scanning, participants completed three additional ratings. They were asked to indicate the extent to which the memories were changed by the 6 repetitions during scanning on a scale ranging from 1 (not at all) to 5 (completely). They reported that the memories were not changed very much by repetition (mean: 2.61, SD: 0.74). They were also asked how often during scanning they

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298 thought about the memory interview one week previous on a scale of 1 (not at all) to 5 (completely),
299 with participants indicating they rarely thought about the interview (mean: 2.29, SD: 1.01). Finally,
300 participants were asked the extent to which the recall of memories from each time period unfolded in a
301 consistent manner over the course of the session. A difference was observed ($F_{(7,203)}$ = 2.78, p = 0.009),
302 with the most recent 0.5M old memories being rated as more consistently recalled than the most
303 remote 60M memories (t_{29} = 3.97, p = 0.012).

304 In addition to the region of interest (ROI)-based approach, a searchlight analysis was also
305 conducted in MNI group normalised space to localise areas within the vmPFC where memories displayed
306 high detectability across participants (see Materials and methods). We discovered a significant bilateral
307 cluster of 652 voxels (see Fig A in S4 Fig), and subsequently used RSA to quantify the strength of neural
308 representations at each time-point within this area (see Fig B in S4 Fig). The results were highly similar to
309 the whole-ROI analysis in native space, suggesting the main result may be driven by more spatially
310 confined activity within the vmPFC. However a searchlight approach is sub-optimal to answer the
311 current research question, as it requires an *a priori* model RSM against which to compare the neural
312 patterns at each searchlight sphere, whereas the ROI approach makes no such assumptions.

313 We also conducted a standard mass-univariate analysis on the whole volume with memory
314 remoteness as a parametric regressor, and no area displayed either a significant increase or decrease in
315 activity in accordance with memory age, consistent with the findings of Bonnici et al. [54]. In a similar
316 parametric analysis, we did not find evidence of the modulation of univariate activity by in-scanner
317 vividness ratings as might be suggested by the findings of Sheldon and Levine [60], however, all
318 memories chosen for the current study were highly vivid in nature.

319 One concern when studying covert cognitive processes such as autobiographical memory in the
320 fMRI scanner is participant compliance, because performance is subjectively reported rather than
321 objectively assessed. However if participants were complying with task demands, there should be an
322 association between in-scanner subjective ratings and the detectability of neural representations. When
323 non-vivid trials were additionally incorporated into the RSA analysis, the mean memory representation

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score in the vmPFC for all participants averaged across time-points decreased from 0.0049 (SD 0.005) to 0.0044 (SD 0.005). In fact, the deleterious effect of including these extra non-vivid trials was evident in 24 out of the 30 participants. Such a consistent relationship between participants' subjective ratings of their own memory performance and the sensitivity of the RSA analysis to detect memory representations, strongly suggests participants were performing the task as instructed.

Rationale and predictions for Experiment 2

The non-monotonic pattern we observed in the fMRI data did not manifest itself in the subjective or objective behavioural data. In fact, the only difference in those data was higher ratings for the most recent 0.5M old memories. However, these were paradoxically the most weakly represented memories in the vmPFC, meaning the neural patterns were not driven by memory quality. The objective scoring of the memories confirmed comparable levels of detail provided for all memories, without any significant drop in episodic detail or increase in the amount of semantic information provided as a function of time. Therefore, the amount or nature of the memory details were not contributing factors.

Nevertheless, to verify that the results genuinely represented the neural correlates of memory purely as a function of age, one would need to study the effects of the passage of time on the individual neural representations. Therefore we invited the participants to revisit eight months later to recall the same memories again both overtly and during scanning; 16 of the participants agreed to return. In order to generate specific predictions for the neural representations during Experiment 2, we took the actual data for the 16 subjects from Experiment 1 who returned eight months later (Fig 5 green line, where the non-monotonic pattern is still clearly evident), and shifted it forwards by two time-points to simulate the expected pattern eight months later (Fig 5 pink dotted line). Note that for the 28M and 32M time periods in Experiment 2 we assumed they would have the same level of detectability as 24M old memories given the absence of data relating to these time periods from Experiment 1. We further assumed the neural representations between 60M and 68M would be unchanged.

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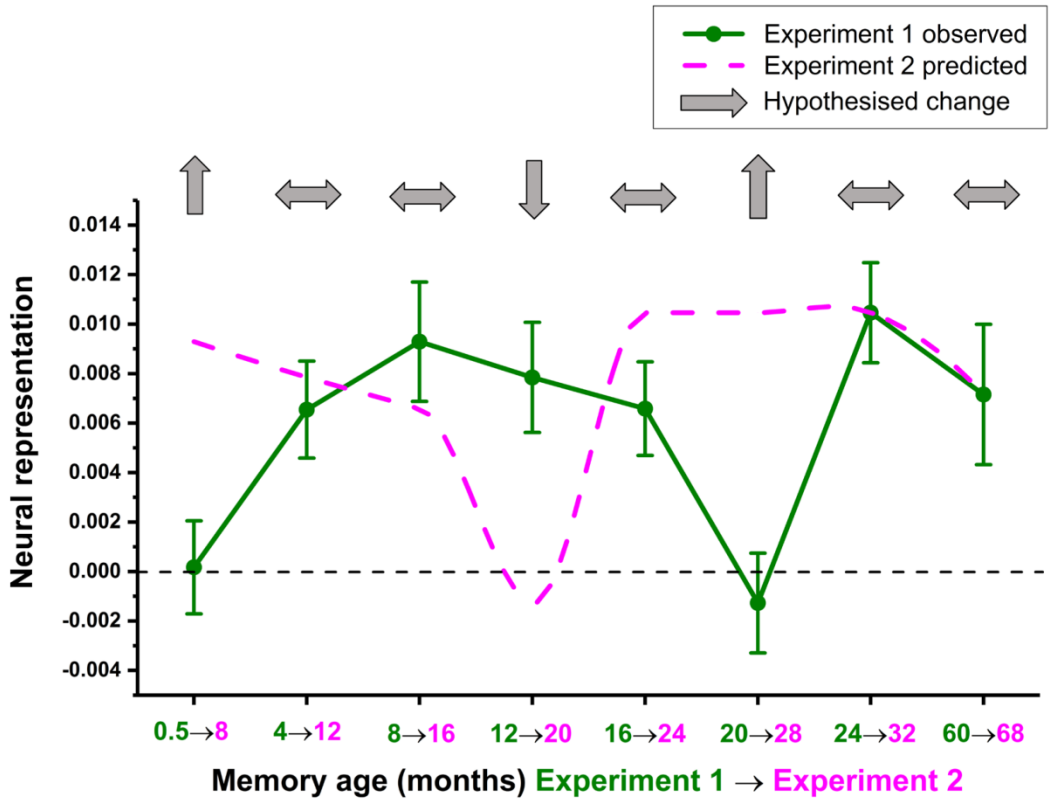

Fig 5. Predicted fMRI changes eight months later in Experiment 2. Predicted changes in the neural representations of individual autobiographical memories after eight months (pink dotted line), based on shifting the original observed data forward by two time-points for the 16 participants from Experiment 1 (green line) who returned for Experiment 2 (see S4 Data for original and predicted values). Light grey arrows indicate the hypotheses.

A comparison of the original and simulated neural representation scores yielded a number of clear hypotheses about how memory representations would change over time in the vmPFC. Two week old memories should become detectable eight months later, while the original 4M and 8M old memories should not differ in their representational strength. Twelve month old memories from Experiment 1 should be significantly less detectable, whereas 16M old memories should remain unchanged. The original 20M old memories should be better represented at 28M, whereas the 24 and 60 month old memories from Experiment 1 were not predicted to change over time.

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367 **Experiment 2 (eight months later)**

368 One week prior to the fMRI scan, with the assistance of the personal photographs and previously chosen
369 phrases which were used as cues in Experiment 1, the participants verbally recalled and rated the
370 characteristics of their autobiographical memories just as they had done eight months previously (see
371 Materials and methods and Fig 6A).

372

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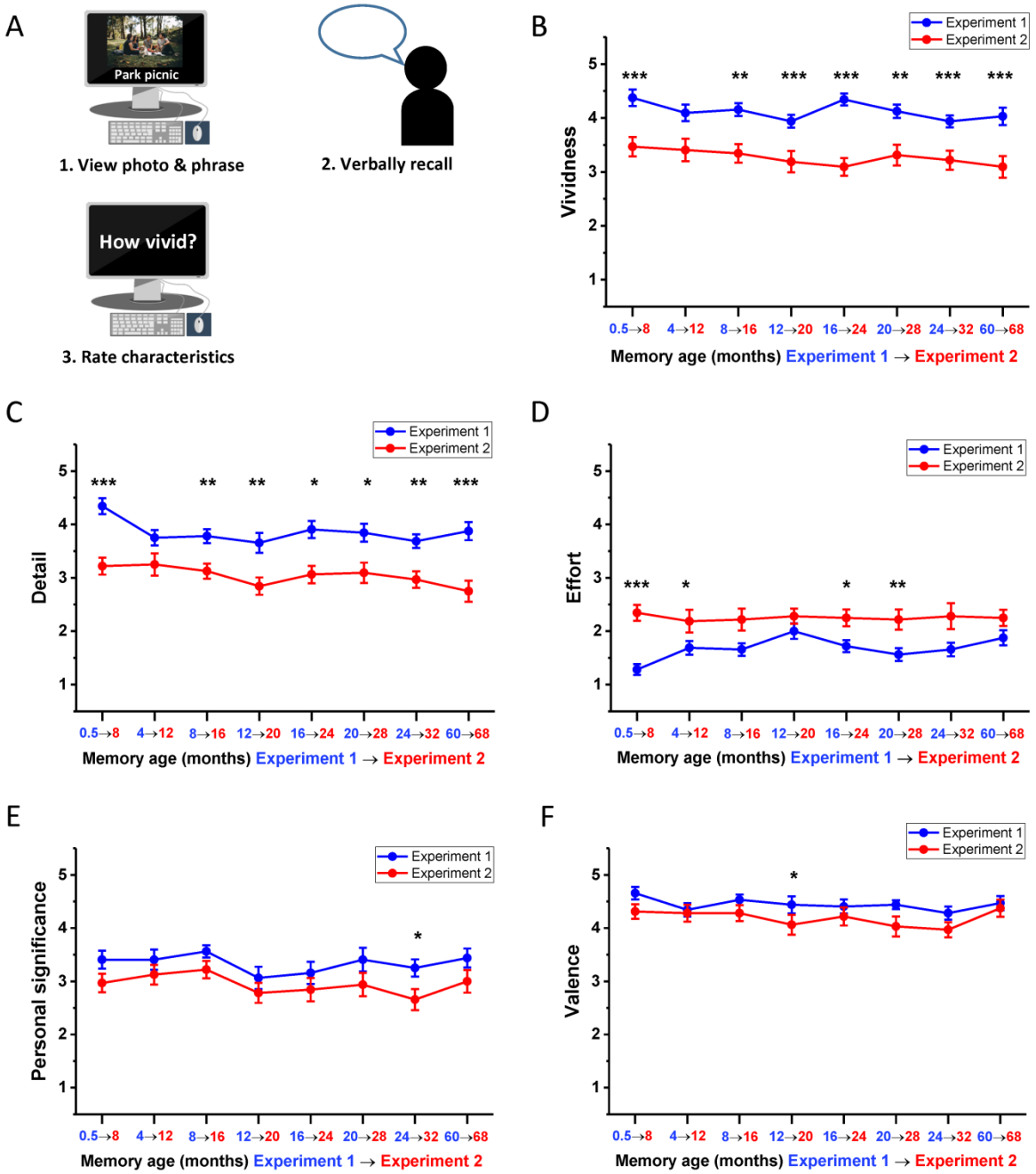

Fig 6. Memory recall and subjective ratings. (A) Schematic of the interview where participants recalled an autobiographical memory using their previously chosen photograph and cue phrase and rated its characteristics. (B-F) Subjective ratings (means +/- 1SEM; see also means and SDs in Table A in S1 Table and Table A in S3 Table) of memory characteristics at each time period for Experiment 1 (blue line, n=16 participants) and how the ratings of the same memories differed eight months later during Experiment 2 (red line, the same n=16 participants) averaged across the two sets of memories in both cases (see S5 Data for individual ratings across both sets of memories). Ratings were on a scale of 1 to 5, where 1 was low and 5 was high. For emotional valence: 1-2 = negative, 3 = neutral, 4-5 = positive. Asterisks indicate significant differences in memory ratings between Experiments 1 and 2; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

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385

386 ***Subjective ratings of phenomenology remain equivalent across memories***

387 Means and SDs are provided in Table A in S3 Table. Autobiographical memories recalled during
388 Experiment 2 did not differ across time periods on vividness ($F_{(7,105)}$ = 0.83, p = 0.564), detail ($F_{(7,105)}$ =
389 1.30, p = 0.257), effort ($F_{(7,105)}$ = 0.11, p = 0.998), personal significance ($F_{(7,105)}$ = 1.49, p = 0.180), valence
390 ($F_{(7,105)}$ = 1.06, p = 0.397), viewpoint ($F_{(3.42,51.22)}$ = 1.24, p = 0.31) or motion ($F_{(3.95,59.32)}$ = 1.43, p = 0.237).
391 When asked how frequently they had thought about the autobiographical memories in the eight months
392 between experiments (rated on a five point scale from "never" to "very frequently"), participants
393 reported some change across time periods ($F_{(7,105)}$ = 3.04, p = 0.006). However, the only significant
394 difference between time periods was a lower recall frequency for now 32M old memories compared to
395 the now 12M (t_{15} = 3.87, p = 0.042). Given the range of responses to this question across conditions
396 (1.50-2.03), clearly participants had not given the memories much thought in the intervening eight
397 months. Therefore, all memories recalled in Experiment 2 were extremely well matched in terms of their
398 phenomenology, which reflects the consistency observed in ratings from eight months onwards in
399 Experiment 1.

400 There were, however, differences in the absolute values of subjective ratings between the two
401 experiments. There was a decrease in the reported vividness of all memories from Experiment 1 to
402 Experiment 2 ($F_{(1,15)}$ = 88.45, p < 0.001), from 0.5M to when they were 8M old (t_{15} = 6.21, p < 0.001), 8M
403 to 16M (t_{15} = 4.21, p = 0.006), 12M to 20M (t_{15} = 5.48, p < 0.001), 16M to 24M (t_{15} = 7.07, p < 0.001), 20M
404 to 28M (t_{15} = 4.10, p = 0.008), 24M to 32M (t_{15} = 5.97, p < 0.001) and 60M to 68M (t_{15} = 5.33, p < 0.001;
405 Fig 6B). A comparable change was observed in the subjective impression of memory detail recalled
406 following the eight month interlude ($F_{(1,15)}$ = 126.81, p < 0.001), with a drop from 0.5M to 8M (t_{15} = 6.26,
407 p < 0.001), 8M to 16M (t_{15} = 4.03, p = 0.009), 12M to 20M (t_{15} = 4.78, p = 0.002), 16M to 24M (t_{15} = 3.72,
408 p = 0.016), 20M to 28M (t_{15} = 3.67, p = 0.018), 24M to 32M (t_{15} = 4.55, p < 0.003) and 60M to 68M (t_{15} =
409 9.67, p < 0.001; Fig 6C). Recalling memories eight months later was also perceived as more effortful
410 ($F_{(1,15)}$ = 43.32, p < 0.001), from 0.5M to 8M (t_{15} = -7.81, p < 0.001), 4M to 12M (t_{15} = -3.30, p = 0.039),

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411 16M to 24M (t_{15} = -1.95, p = 0.021), and 20M to 28M (t_{15} = -4.03, p = 0.009; Fig 6D). The elapsed time
412 between experiments also led to a reduction in the reported personal significance of memories ($F_{(1,15)}$ =
413 11.82, p = 0.004), from 24M to 32M (t_{15} = 3.58, p = 0.022; Fig 6E). Ratings of emotional valence also
414 changed over the eight month period ($F_{(1,15)}$ = 9.78, p = 0.007), with a reported attenuation of the
415 positivity of memories from 12M to 20M (t_{15} = 3.87, p = 0.012; Fig 6F). In addition to these main ratings,
416 no difference was reported in the extent to which memories were recalled from a first or third person
417 perspective ($F_{(1,15)}$ = 0.513, p = 0.485) over the eight month period. The extent to which memories were
418 recalled as active or static was altered by the passage of time between experiments ($F_{(1,15)}$ = 11.01, p =
419 0.005), with the original 0.5M old memories becoming more static when 8M old (t_{15} = -3.42, p = 0.031).
420 See S12 Data for individual ratings for these characteristics.

421 Despite the observed changes in some subjective ratings from Experiment 1 to Experiment 2,
422 they were unidirectional across all time periods. As such, if the pattern of hypothesised emergence and
423 disappearance of neural representations in vmPFC were to be supported in Experiment 2, then it could
424 not be accounted for by changes in subjective ratings. Additionally, although the changes in subjective
425 ratings across time tend to suggest a comparable degradation in memory quality across all time periods,
426 this may be misleading. The ratings overall were still high, and these absolute changes in values could be
427 influenced by participants' expectations of their ability to recall memories after an extended period of
428 time with high fidelity, because the objective scoring of memory detail revealed no such pattern, as we
429 report in the next section.

430

431 ***A similar level of detail was recalled across experiments***

432 As with Experiment 1, transcripts of participants' memory interviews during Experiment 2 were scored
433 using the Autobiographical Interview protocol ([57]; see Materials and methods)). A total of 6,444
434 details were scored (see Table B in S3 Table for means, SD). There was a difference in the number of
435 details recalled across different time periods in Experiment 2 ($F_{(7,105)}$ = 2.49, p = 0.021). However, this
436 difference was only observed for external details ($F_{(7,105)}$ = 3.25, p = 0.004), with more provided for 28M

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437 memories than 12M memories (t_{15} = -4.68, p = 0.008). As with Experiment 1, the number of internal and
438 external details differed ($F_{(1,15)}$ = 72.57, p < 0.001), with more internal details recalled for every time
439 period (all p < 0.01). No interaction between time period and type of detail was observed ($F_{(7,105)}$ = 0.87,
440 p = 0.530).

441 When the objective scores for both experiments were compared, no significant difference was
442 observed in the overall number of details provided eight months later ($F_{(1,15)}$ = 1.93, p = 0.185; Fig 7).
443 Furthermore, there was no significant interaction between experiment and time period ($F_{(1,15)}$ = 1.97, p =
444 0.066), indicating that the amount of details provided for memories from any particular time period in
445 Experiment 1 were not affected by the passage of time. Finally, no interaction was observed between
446 experiment and type of detail provided ($F_{(1,15)}$ = 2.27, p = 0.153), showing that the ratio of internal to
447 external details was preserved across experiments.

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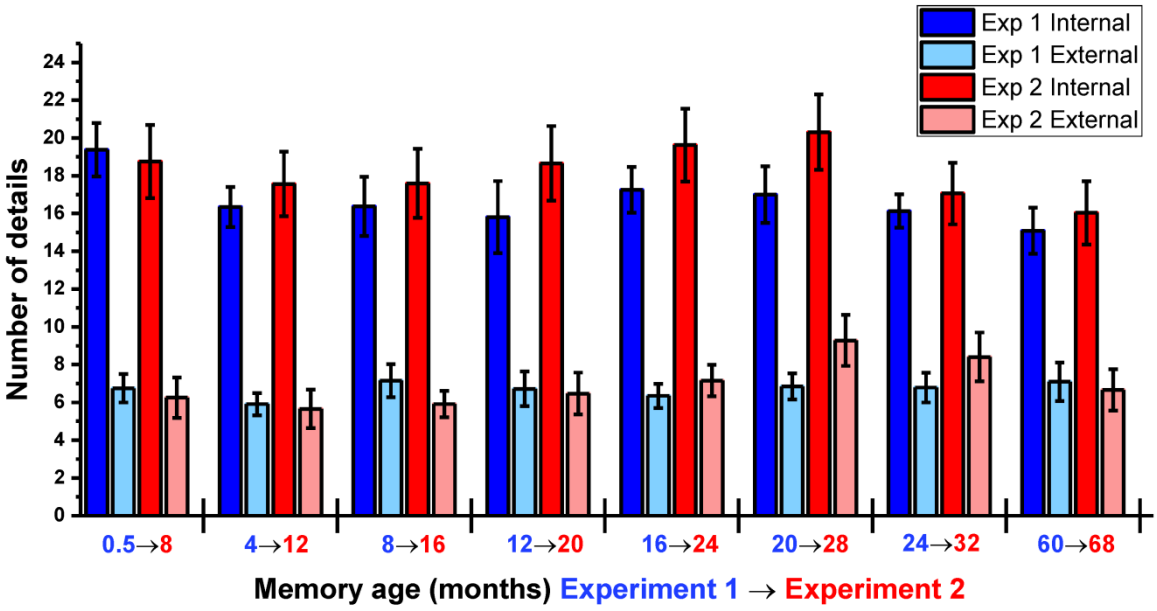

449
450
451 **Fig 7. Objective scores for memory details over time.** The mean +/- 1SEM (see also means and SDs in Table B in S1
452 Table and Table B in S3 Table) number of internal and external details at each time period for Experiment 1 (blue
453 bars, n=16 participants) and Experiment 2 (red bars, the same n=16 participants), averaged across the two sets of
454 autobiographical memories (see S6 Data for individual participant scores).
455
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461 ***vmPFC memory representations undergo the predicted time-dependent changes***

462 Participants were scanned in an identical fashion as Experiment 1 (see Materials and methods and Fig
463 3B), and neural representation scores for memories from each time point were again calculated.

464 When comparing the neural representation scores of memories from the eight original time
465 periods in Experiment 1 with those of the same memories eight months later during Experiment 2, a
466 main effect for experiment ($F_{(1,15)}$ = 2.35, p = 0.146), or time period ($F_{(7,105)}$ = 1.18, p = 0.323), was not
467 observed, however, an interaction between experiment and time period emerged ($F_{(7,105)}$ = 3.46, p =
468 0.002). Closer examination via our planned comparisons (Fig 8A) revealed that seven out of the eight
469 predictions made on the basis of the Experiment 1 findings were supported (Fig 8B). The original 0.5M
470 old memories had increased in their representational strength in vmPFC eight months later (t_{15} = -1.84, p
471 = 0.043), while the neural representation scores of the 4M and 8M old memories were essentially
472 unchanged at 12M (t_{15} = 0.43, p = 0.677) and 16M (t_{15} = 1.22, p = 0.242) respectively. As expected, the
473 original 12M old memories from Experiment 1 were eight months later more poorly represented in
474 vmPFC when 20M months old (t_{15} = 1.85, p = 0.042). The original 16M old memories were unchanged in
475 their representational strength at 24M (t_{15} = 1.38, p = 0.187), while 20M old memories were significantly
476 more detectable in vmPFC at 28M (t_{15} = -2.69, p = 0.008). The most remote 60M memories did not differ
477 in their neural representation scores eight months later (t_{15} = 0.86, p = 0.402). In fact the only finding
478 which was inconsistent with the predictions generated by Experiment 1 was a decrease in the
479 representation of 24M old memories when they were 32M of age (t_{15} = -2.69, p = 0.009). However, this
480 prediction was based on the assumption that memories do not undergo further dynamic shifts in neural
481 representation between two and five years, which may not be the case, and we did not have 32M data
482 from Experiment 1 to corroborate this finding.

483

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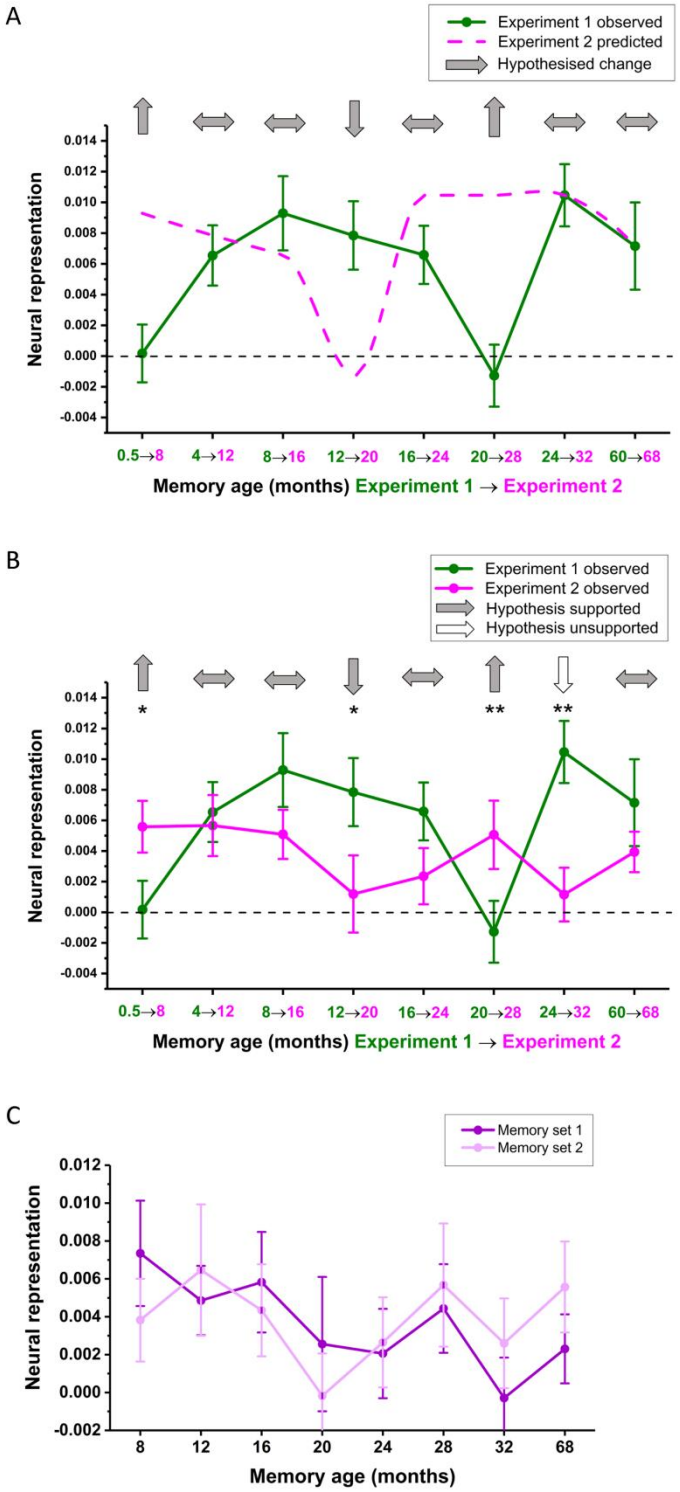

Fig 8. fMRI results of Experiment 2. (A) A reminder of the hypothesised changes in neural representations from Experiment 1 (green line) to Experiment 2 (pink line, reprinted from Fig 5). (B) Mean +/- 1SEM neural representation scores at each time-point averaged across the two sets of memories for Experiment 2 (pink line, n=16 participants) compared to the same memories from eight months previously (green line, the same n=16 participants). Light grey and white arrows indicate supported and unsupported hypotheses respectively; * $p < 0.05$, ** $p < 0.01$. (C) Neural representation scores at each time-point for Experiment 2, plotted separately for the two sets of autobiographical memories. See S7 data for individual participant scores.

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For completeness, Fig 8C plots the neural representation scores for the two sets of memories in Experiment 2. As previously observed in Experiment 1, the two sets of memories displayed a similar time-course in terms of their neural representations, despite being recalled in separate scanning sessions, in a randomised order and analysed separately. As with Experiment 1, when examining other brain areas within the partial volume in Experiment 2, in no case did we find a significant difference in memory detectability across time periods.

Following scanning in Experiment 2, participants completed three additional ratings. They were asked to indicate the extent to which the memories were changed by the 6 repetitions during scanning on a scale ranging from 1 (not at all) to 5 (completely). As in Experiment 1, they reported that the memories were not changed very much by repetition (mean: 2.56, SD: 0.81). They were also asked how often they thought of the experience of recalling the memories in Experiment 1 while performing the scanning task in Experiment 2 on a scale of 1 (not at all) to 5 (during every memory). Participants indicated they rarely thought about Experiment 1 (mean: 1.75, SD: 0.93). Finally, the consistency of recall across time periods during the scanning session did not differ in Experiment 2 ($F_{(7,105)} = 0.59$, $p = 0.761$) or between the two experiments ($F_{(1,15)} = 0.12$, $p = 0.733$; see also Table A in S1 Table and Table A in S3 Table).

Discussion

This study exploited the sensitivity of RSA to detect not only the extent to which memories of different ages were represented in the vmPFC, but how these representations changed over time. During Experiment 1, we observed detectability in vmPFC for memories at 4M to 12M of age, which was also evident at 24M and 60M. As expected, recent 0.5M old memories were poorly represented in vmPFC in comparison. Curiously, however, the same lack of detectability in vmPFC was observed for memories that were 16M to 20M old. This pattern persisted across separate sets of memories and was replicated in a follow-up study eight months later with the same participants and memories. Behavioural data failed to account for these time-dependent representational changes in either experiment and other

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519 regions failed to show a significant change in memory representations over time. These findings are
520 difficult to accommodate within any single theoretical account of long-term memory consolidation [9,
521 12, 61-63], as neocortical recruitment is generally assumed to involve an ascending linear trajectory.
522 Consolidation has been characterised as fluid and continuous [64], but the non-monotonic vmPFC
523 engagement observed here suggests additional complexity in its temporal recruitment.
524
525 **Possible mechanisms underlying non-monotonic vmPFC recruitment**
526 Over the course of consolidation in this study, the vmPFC twice alternated between disengagement and
527 engagement, indicative of four separate stages. Below we consider, based on the latest theoretical
528 developments and empirical research on systems-level consolidation and vmPFC functioning, the time-
529 dependent processes which could underlie such a non-monotonic pattern.
530
531 ***Less than one month: quiescence during the early stages of systems-level consolidation***
532 During retrieval of memories less than one month of age, there was a notable absence of vmPFC
533 recruitment. This is consistent with previous human studies showing weaker representations of recent
534 memories using pattern classification [54], and lower overall levels of fMRI activity [41]. Similarly, in
535 animals, prefrontal activation is reduced during recent memory recall [18, 19], with lesions of this region
536 generally preserving recent memory retrieval [21, 24]. Although prefrontal cells may be 'tagged' for
537 subsequent consolidation around the time of encoding [14], they remain functionally immature and do
538 not appear to significantly contribute to memory retrieval at this stage [26].
539
540 ***Four months to one year: disambiguation of competing consolidated representations***
541 Over the subsequent three time periods in this study, vmPFC memory representations progressively
542 strengthened. This echoes the time-dependent increases in prefrontal cortex activity observed in animal
543 studies during memory retrieval [19, 65], and the disruption of remote memory following prefrontal
544 inactivation [19, 21, 24]. While it has been demonstrated that the interim replay of recent experiences in

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545 the prefrontal cortex [66] coincides with lasting structural changes which facilitate subsequent recall
546 [29], it is still unclear how these consolidated representations are utilised during retrieval. One
547 prominent hypothesis is that the prefrontal cortex suppresses irrelevant representations [67], with
548 corresponding evidence in animals that context-inappropriate memories are triggered following
549 prefrontal inactivation [68]. Similarly in humans, vmPFC damage impairs the ability to suppress
550 inappropriate memories through confabulation [34], and produces a tendency to confuse memories
551 which have taken place in different contexts [69]. This is of potential relevance to the four to twelve
552 month time period identified in the current study, as people remember vastly more memories from the
553 past year than more remote life periods [70]. Therefore, the demands on memory disambiguation (the
554 ability to correctly select from among similar memories during retrieval) are significantly increased
555 across this timescale. For example, in attempting to recall the specific events from a party one attended
556 months previously, multiple contemporaneous experiences which involve the same people, or have
557 taken place in a similar context could interfere with recollection. While humans possess a large capacity
558 for real-world stimuli in recent memory, an abundance of stored competing representations can be
559 detrimental to memory performance during retrieval [71]. Therefore, vmPFC recruitment at these time-
560 points may reflect a suppression of distractor representations which are inappropriate to the current
561 retrieval intentions. Importantly, this would be a memory-specific process which would generate a
562 consistent neural pattern every time a particular experience is recalled.
563
564 ***Sixteen to 20 months: time-induced decay negates the need for disambiguation***
565 The progressive vmPFC disengagement observed over the following eight months suggests the
566 suppression of interfering memories becomes less of a necessity over this period. Forgetting is a key
567 attribute of an optimally functioning memory system [72], and the number of autobiographical events
568 individuals can recall has been shown to decrease substantially between one and two years, before
569 levelling off [73]. Therefore, the reduction in availability of potentially interfering memories from this
570 time period may relieve the vmPFC from its role in disambiguating them from memories which have

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571 persisted through the consolidation process. For example, one may return from a vacation with many
572 memories which contain multiple overlapping features, but this will inevitably be reduced to a few
573 distinct experiences as time goes on.
574
575 ***Two years to five years: the emergence of schematic representations***
576 If disambiguation ceases to be an issue for older memories, the robust re-engagement of vmPFC at more
577 remote time periods suggests locally consolidated representations come to be used in a different way to
578 assist in recall. From a theoretical perspective, systems-level consolidation is no longer viewed as the
579 time-limited stabilisation of a static engram. Rather, the passage of time and repeated retrieval is
580 thought to generate an additional representation which can complement the original detailed memory
581 [10]. This emergent representation is schematic in nature, with an emphasis on general rather than
582 specific details, and forms part of a flexible memory system which adapts to current demands. The
583 network hub which supports schematic representations, suggested by both animal [17] and human
584 neuroimaging [74] studies, is the medial prefrontal cortex. Further evidence is provided by patients with
585 vmPFC lesions, who are resistant to false memory effects because schemas which would conflate
586 actually studied and similar unseen words are not activated during retrieval [75]. Therefore, it is likely
587 that the nature of memory representations in the vmPFC transform over the course of consolidation to
588 become more schematic in nature. Accordingly, the re-engagement of vmPFC activity at more remote
589 time-points in this study could point to the deployment of memory-congruent schema to assist in
590 retrieval. For example, the vivid recollection of a memory from five years previously will likely require
591 reorientation to an increasingly unfamiliar environment, an altered social network, and a different
592 personal mindset. This may be facilitated by a rapid instantiation of relevant schematic representations
593 in the vmPFC to bias retrieval in posterior brain regions, as proposed by Gilboa and Marlatte [76]. The
594 non-monotonic recruitment observed here may, therefore, reflect not just the consolidation of neural
595 representations, but their evolution over time and, most importantly, the way in which they are used to
596 facilitate precise and holistic recollection. Importantly, vmPFC engagement during recall likely reflects

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not just task-related recruitment, but also communication with the hippocampus and other neocortical regions.

Relevance to systems-level consolidation theories

The current findings have potential implications for the two dominant theoretical perspectives on systems-level consolidation. Standard Consolidation Theory [7] predicts that the passage of time promotes the strengthening of neural representations in the neocortex, but the duration of this process in humans is poorly specified. The current results suggest this process is accomplished over a relatively fast timescale on the order of months. The alternative perspective on consolidation, Multiple Trace Theory and Transformation Hypothesis [10], posits that over time, consolidation promotes the emergence of schematic, gist-like representations in the neocortex, which complement the original detailed memory. The re-engagement of the vmPFC at two years in this study may reflect the emergence of these generalised representations to facilitate specific recall at more remote time-points. Therefore, the consolidation of new memories in the neocortex may be reasonably rapid, whereas the transformation of these engrams may take place over a much longer timescale.

Using an autobiographical memory paradigm to study consolidation is preferable to laboratory-based episodic memory tests by virtue of its ecological validity, availability of temporally distant stimuli, clinical significance and context-dependent equivalence to animal tasks. However, studying autobiographical memory carries with it potential confounds which can affect interpretation of results. Below we consider why these factors cannot account for our observations.

Consistency of recall and forgetting

Older memories may yield a higher RSA score if they are more consistently recalled. Here, however, participants actually rated 0.5M memories as more consistently recalled than 60 month old memories. Older memories were not impoverished in detail when compared to the detail available for recent

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623 memories. Moreover, an inspection of interview transcripts across experiments revealed participants
624 rarely offered new details for previous memories when retested, countering the suggestion that
625 increased detectability of old memories may arise from the insertion of new episodic or semantic details
626 [77]. The consistency in recalled detail across experiments could be attributable to participants recalling
627 in Experiment 2 what they had said during Experiment 1. However whether or not participants
628 remembered by proxy is irrelevant, as they still recalled the specific details of the original event,
629 removing forgetting as a potential explanation of changes in neural patterns over time.
630
631 **The influence of repetition**
632 Retrieving a memory initiates reconsolidation, a transient state where memories are vulnerable to
633 interference [78, 79]. Therefore, repeated retrieval may cause this process to have an influence on
634 neural representations. However, all memories were recalled one week before the fMRI scan, so if such
635 an effect was present it would be matched across time-points. Retrieval at this stage may also accelerate
636 consolidation [80], yet if this was a major influence, we would likely have found 0.5M memories to be
637 more detectable than they were. Further repetition of memories within the scanner in Experiment 1
638 took place over a timescale that could not affect consolidation processes or interpretation of the initial
639 neural data. Nevertheless, this could arguably affect vmPFC engagement over a longer period of time
640 [81] and thus perturb the natural course of consolidation, influencing the results of Experiment 2.
641 However, given that seven out of the eight specifically hypothesised temporally sensitive changes in
642 neural representations were supported, an altered or accelerated consolidation time-course appears
643 highly unlikely. Again, recall recency was matched in Experiment 2 by the memory interview, and recall
644 frequency between experiments was low.
645 Taking a more general and parsimonious perspective, the ratings demonstrate that, naturally, all
646 memories are recalled on an occasional basis (Table A in S1 Table), therefore it seems highly unlikely
647 that a mere six repetitions within a scanning session would significantly alter the time course of systems-
648 level consolidation. It should also be noted that successful detection of neural patterns relied on the

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649 specific content of each memory, rather than being due to generic time-related retrieval processes (S4
650 Fig). One alternative to the current two-experiment longitudinal design to limit repetition across
651 experiments would be to have a different group of participants with different memories for the second
652 experiment. However the strength of the current approach was the ability to track the transformation in
653 neural patterns of the same memories over time.
654
655 **The effect of selection**
656 An alternative interpretation of the time-sensitive vmPFC engagement is a systematic bias in the content
657 of selected memories. For example, annual events coinciding across all participants, such as a seasonal
658 holiday. However, recruitment took place over a period of five months in an evenly spaced manner,
659 ensuring that such events did fall into the same temporal windows across participants. The occurrence
660 of personal events such as birthdays was also random across participants. The use of personal
661 photographs as memory cues also limited the reliance on time of year as a method for strategically
662 retrieving memories. Furthermore, the nature of memory sampling was that unique, rather than generic,
663 events were eligible, reducing the likelihood of events which were repeated annually being included.
664 Memory detectability was high at 12 month intervals such as one, two and five years in this study,
665 suggesting perhaps it is easier to recall events which have taken place at a similar time of year to the
666 present. However this should have been reflected in behavioural ratings, and equivalently strong neural
667 representations for recent memories, but neither was observed. Most importantly, if content rather
668 than time-related consolidation was the main influence on memory detectability, then we would not
669 have observed any change in neural representation scores from Experiment 1 to Experiment 2, rather
670 than the hypothesised shifts which emerged.
671 A related concern is that memories across time differ in nature because they differ in availability.
672 Successful memory search is biased towards recency, meaning there are more events to choose from in
673 the last few weeks, than remote time periods. Here, this confound is circumvented by design, given that
674 search was equivalently constrained and facilitated at each time-point by the frequency at which

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675 participants took photographs, which was not assumed to change in a major way over time. These
676 enduring "snap-shots" of memory, located within tight temporal windows (see Materials and methods)
677 meant that memory selection was not confounded by retrieval difficulty or availability. It could also be
678 argued that selection of time-points for this study should have been biased towards recency given that
679 most forgetting occurs in the weeks and months after learning. However, it is important to dissociate
680 systems-level consolidation from forgetting, as they are separate processes which are assumed to follow
681 different time-courses. Memory forgetting follows an exponential decay [82], whereas systems-level
682 consolidation has generally been assumed, until now, to be gradual and linear [83]. Our study was
683 concerned only with vivid, unique memories which were likely to persist through the systems-level
684 consolidation process.

685 A further potential concern regarding memory selection is that recent and remote memories
686 which are comprised of equivalent levels of detail must be qualitatively different in some way. For
687 example, selected remote memories must have been highly salient at the time of encoding to retain
688 such high levels of detail. However, the underlying assumption that individual memories invariably
689 become detail impoverished over time does not necessarily hold. While the volume of memories one
690 can recall decreases over time [84], the amount of details one can recall from individual consolidated
691 memories can actually increase over a one year delay [85]. While generalised representations are
692 thought to emerge over the course of consolidation, they do not necessarily replace the original detailed
693 memories [10], and the equivalent level of detail provided by participants across the two experiments
694 here would suggest that memory specificity can be preserved over time. Furthermore, the possibility
695 that remote memory selection may still be biased towards more salient memories is rendered unlikely
696 by the method of memory sampling employed here. Because memories were chosen only from available
697 photographic cues, the salience of recent and remote events was determined at the time of taking the
698 photograph, and not during experimentation. These photographs served as potent triggers of remote
699 memories which were not necessarily more salient than recent memories, and which may not have
700 otherwise come to mind using a free recall paradigm. In addition, one would expect more salient remote

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701 memories to score higher than recent memories on subjective ratings of vividness, personal significance
702 or valence, but this was not the case. Therefore, stronger neural representations at more remote time-
703 points were likely due to consolidation-related processes rather than qualitative difference between
704 recent and remote experiences at the time of encoding.
705
706 **Value**
707 Given that the medial prefrontal cortex is often associated with value and emotional processing [86],
708 could these factors have influenced the current findings? Humans display a bias towards consolidating
709 positive memories [87], and remembered information is more likely to be valued than that which is
710 forgotten [88]. Activity in vmPFC during autobiographical memory recall has been found to be
711 modulated by both the personal significance and emotional content of memories [89]. However, in the
712 current two experiments, memories were matched across time periods on these variables, and the
713 selection of memories through photographs taken on a day-to day basis also mitigated against this
714 effect. In the eight months between experiments, memories either remained unchanged or decreased
715 slightly in their subjective ratings of significance and positivity, suggesting that these factors are an
716 unlikely driving force behind the observed remote memory representations in vmPFC. For example, if
717 recent memories in Experiment 1 were not well-represented in vmPFC because they were relatively
718 insignificant, there is no reason to expect them to be more so eight months later, yet their neural
719 representation strengthened over time nonetheless.
720
721 **Relation to previous findings**
722 A methodological discrepancy between this experiment and that conducted by Bonnici et al. [54], is the
723 additional use of a photograph to assist in cueing memories. One possible interpretation of the neural
724 representation scores is they represent a role for the vmPFC in the maintenance of visual working
725 memory following cue offset. However, the prefrontal cortex is unlikely to contribute to maintenance of

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726 visual information [90]. Furthermore, if this was the driving effect behind neural representations here,
727 the effect would be equivalent across time-periods, yet it was not.

728 There is, however, an obvious inconsistency between the findings of the current study and that
729 of Bonnici, et al. [54]. Unlike that study, we did not detect representations of 0.5M old memories in
730 vmPFC. It could be that the support vector machine classification-based MVPA used by Bonnici et al. [54]
731 is more sensitive to detection of memory representations than RSA, however, the current study was not
732 optimised for such an analysis because it necessitated an increased ratio of conditions to trials.
733 Nonetheless, the increase in memory representation scores from recent to remote memories was
734 replicated and additionally refined in the current study with superior temporal precision. One
735 observation which was consistent with the Bonnici findings was the detection of remote memories in the
736 hippocampus, which also supports theories positing a perpetual role for this region in the vivid retrieval
737 of autobiographical memories [10, 12]. However, the weak detectability observed at more recent time
738 points may reflect a limitation of the RSA approach employed here to detect sparsely encoded
739 hippocampal patterns, which may be overcome by a more targeted subfield analysis [91].

740 There are, however, distinct advantages to the use of RSA over pattern classification MVPA. RSA
741 is optimal for a condition-rich design as it allows for the relationships between many conditions to be
742 observed. For example, in the current experiment, a visual inspection of the group RSA matrix (S1 Fig)
743 does not reveal an obvious clustering of recent or remote memories which would indicate content-
744 independent neural patterns related to general retrieval processes. The approach employed by Bonnici
745 et al. [54] assessed the distinctiveness of memories within each time-point from each other in order to
746 detect memory representations. Should the neural patterns of a single memory become more consistent
747 over time, yet also more similar to memories of the same age due to generic time-dependent
748 mechanisms of retrieval, pattern classification would fail to detect a representation where one is
749 present. In the current study, however, the two can be assessed separately, revealing memories at each
750 time-point become distinct from both memories of all other ages (Fig 4A) and identically aged memories
751 (Fig 4C). The machine learning approach employed by Bonnici et al. [54] to decode memory

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752 representations also requires the division of data into 'training' and 'testing' sets to classify unseen
753 neural patterns [53]. This reduces the number of trials available for analysis, which would have been
754 suboptimal for the current design because it would have necessitated an increased number of conditions
755 and fewer trials per memory, whereas this restriction is not a necessity for RSA. Finally, because the
756 pattern classification approach used by Bonnici et al. [54] compared memories from each time-point
757 directly to each other, they could not be analysed independently. In the current RSA design, the two sets
758 of memories could be analysed separately from each other to ascertain if the temporal patterns could be
759 replicated in an independent set of data. As is evident in Fig 4B, the non-monotonic pattern of vmPFC
760 recruitment was present in both sets of memories. The suitability of each MVPA method, therefore,
761 depends on the study design and the research questions being posed.

762 In the light of our hypotheses, Experiment 2 generated one anomalous finding. Twenty-four
763 month old memories from Experiment 1 were no longer well represented eight months later. Why
764 memories around 32M of age are not as reliant on vmPFC is unclear, but unlike other time-periods, we
765 cannot verify this finding in the current experiment, as we did not sample 32M memories during
766 Experiment 1.

767

768 **Summary**

769 The current results revealed that the recruitment of the vmPFC during the expression of
770 autobiographical memories depends on the exact stage of systems-level consolidation, and that retrieval
771 involves multiple sequential time-sensitive processes. These temporal patterns were remarkably
772 preserved across completely different sets of memories in one experiment, and closely replicated in a
773 subsequent longitudinal experiment with the same participants and memories. These findings support
774 the notion that the vmPFC becomes increasingly important over time for the retrieval of remote
775 memories. Two particularly novel findings emerged. First, this process occurs relatively quickly, by four
776 months following an experience. Second, vmPFC involvement after this time fluctuates in a highly
777 consistent manner, depending on the precise age of the memory in question. Further work is clearly

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778 needed to explore the implications of these novel results. Overall, we conclude that our vmPFC findings
779 may be explained by a dynamic interaction between the changing strength of a memory trace, the
780 availability of temporally adjacent memories, and the concomitant differential strategies and schemas
781 that are deployed to support the successful recollection of past experiences.

782

783 Materials and methods

784 Ethics statement

785 This study was approved by the local research ethics committee (University College London Research
786 Ethics Committee, approval reference 6743/002). All investigations were conducted according to the
787 principles expressed in the Declaration of Helsinki. Written informed consent was obtained for each
788 participant.

789

790

791

792 Experiment 1

793 *Participants*

794 Thirty healthy, right handed participants (23 female) took part (mean age 25.3, SD 3.5, range 21-32).
795 All had normal or corrected-to-normal vision.

796

797 *Memory interview and selection of autobiographical memories*

798 Participants were instructed to select at least three photographs from each of eight time-points in their
799 past (0.5M, 4M, 8M, 12M, 16M, 20M, 24M and 60M relative to the time of taking part in the
800 experiment) which reminded them of vivid, unique and specific autobiographical events. The sampling
801 was retrospective, in that the photographs were chosen from the participants' pre-existing photograph
802 collections and not prospectively taken with the study in mind. Highly personal, emotionally negative or

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803 repetitive events were deemed unsuitable. An additional requirement was that memories from the
804 same time period should be dissimilar in content. For the four most recent time periods (0.5M-12M), the
805 memories should have taken place within a temporal window two weeks either side of the specified
806 date yielding a potential window of one month, for the next three time points (16M-24M), three weeks
807 either side to allow a window of six weeks, and one month either side for the most remote time point
808 (60M), giving a two month window. This graded approach was adopted to balance temporal precision
809 with the availability of suitable memories at more remote time-points.

810 Participants were asked to describe in as much detail as possible the specific autobiographical
811 memory elicited by a photograph. General probes were given by the interviewer where appropriate
812 (e.g., "what else can you remember about this event?"). Participants were also asked to identify the
813 most memorable part of the event which took place within a narrow temporal window and unfolded in
814 an event-like way. They then created a short phrase pertaining to this episode, which was paired with
815 the photograph to facilitate recall during the subsequent fMRI scan (Fig 1A). Participants were asked to
816 rate each memory on a number of characteristics (see main text, Figs 1 and 6, S1 Table and S3 Table),
817 and two memories from each time period which satisfied the criteria of high vividness and detail, and
818 ease of recall were selected for recollection during the fMRI scan.

819

820 ***Behavioural analyses***

821 The interview was recorded and transcribed to facilitate an objective analysis of the details, and the
822 widely-used Autobiographical Interview method was employed for scoring [57]. Details provided for
823 each memory were scored as either "internal" (specific events, temporal references, places, perceptual
824 observations and thoughts or emotions) or "external" (unrelated events, semantic knowledge, repetition
825 of details or other more general statements). To assess inter-rater reliability, a subset of sixteen
826 memories (n=2 per time period) were randomly selected across 16 different subjects and scored by
827 another experimenter blind to the aims and conditions of the study. Intra-class coefficient estimates

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were calculated using SPSS statistical package version 22 (SPSS Inc, Chicago, IL) based on a single measures, absolute-agreement, 2-way random-effects model.

As two memories per time period were selected for later recall in the scanner, behavioural ratings were averaged to produce one score per time period. Differences in subjective memory ratings across time periods were analysed using a one-way repeated measures ANOVA with Bonferroni-corrected paired t-tests. Differences in objective memory scores of internal and external details across time periods were analysed using a two-way repeated measures ANOVA with Bonferroni-corrected paired t-tests. A threshold of $p < 0.05$ was used throughout both experiments. All ANOVAs were subjected to Greenhouse-Geisser adjustment to the degrees of freedom if Mauchly's sphericity test identified that sphericity had been violated.

Task during fMRI scanning

Participants returned approximately one week later (mean 6.9 days, SD 1) to recall the memories while undergoing an fMRI scan. Prior to the scan, participants were trained to recall each of the 16 memories within a 12 second recall period (as in Bonnici et al. [54], Bonnici and Maguire [55]), when cued by the photograph alongside its associated cue phrase. There were two training trials per memory, and participants were asked to vividly and consistently recall a particular period of the original event which unfolded across a temporal window matching the recall period.

During scanning, participants recalled each memory six times (6 trials x 16 memories = 96 trials). The two memories from each time period were never recalled together in the same session, nor was any one memory repeated within each session, resulting in 12 separate short sessions with eight trials in each, an approach recommended for optimal detection of condition-related activity patterns using MVPA [92]. Trials were presented in a random order within each session. On each trial, the photograph and associated pre-selected cue phrase relating to each event were displayed on screen for three seconds. Following removal of this cue, participants then closed their eyes and recalled the memory. After 12 seconds, the black screen flashed white twice, to cue the participant to open their eyes. The

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854 participant was then asked to rate how vivid the memory recall had been using a five-key button box, on
855 a scale of 1-5, where 1 was not vivid at all, and 5 was highly vivid. When the least vivid trials were
856 excluded, the mean number of trials (/6) selected for analysis from each time-point were as follows:
857 0.5M: 5.65 (SD 0.57), 4M: 5.50 (SD 0.56), 8M: 5.43 (SD 0.55), 12M: 5.50 (SD 0.63), 16M: 5.50 (SD 0.59),
858 20M: 5.43 (SD 0.65), 24M: 5.42 (SD 0.56), 60M: 5.23 (SD 0.69).
859
860 ***MRI data acquisition***
861 Structural and functional data were acquired using a 3T MRI system (Magnetom TIM Trio, Siemens
862 Healthcare, Erlangen, Germany). Both types of scan were performed within a partial volume which
863 incorporated the entire extent of the ventromedial prefrontal cortex (Fig 3A).
864 Structural images were collected using a single-slab 3D T2-weighted turbo spin echo sequence
865 with variable flip angles (SPACE) [93] in combination with parallel imaging, to simultaneously achieve a
866 high image resolution of ~500 μm, high sampling efficiency and short scan time while maintaining a
867 sufficient signal-to-noise ratio (SNR). After excitation of a single axial slab the image was read out with
868 the following parameters: resolution = 0.52 x 0.52 x 0.5 mm, matrix = 384 x 328, partitions = 104,
869 partition thickness = 0.5 mm, partition oversampling = 15.4%, field of view = 200 x 171 mm 2, TE = 353
870 ms, TR = 3200 ms, GRAPPA x 2 in phase-encoding (PE) direction, bandwidth = 434 Hz/pixel, echo spacing
871 = 4.98 ms, turbo factor in PE direction = 177, echo train duration = 881, averages = 1.9. For reduction of
872 signal bias due to, for example, spatial variation in coil sensitivity profiles, the images were normalized
873 using a prescan, and a weak intensity filter was applied as implemented by the scanner's manufacturer.
874 To improve the SNR of the anatomical image, three scans were acquired for each participant,
875 coregistered and averaged. Additionally, a whole brain 3D FLASH structural scan was acquired with a
876 resolution of 1 x 1 x 1 mm.
877 Functional data were acquired using a 3D echo planar imaging (EPI) sequence which has been
878 demonstrated to yield improved BOLD sensitivity compared to 2D EPI acquisitions [94]. Image resolution
879 was 1.5mm^3 and the field-of-view was 192mm in-plane. Forty slices were acquired with 20%

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880 oversampling to avoid wrap-around artefacts due to imperfect slab excitation profile. The echo time (TE)
881 was 37.30 ms and the volume repetition time (TR) was 3.65s. Parallel imaging with GRAPPA image
882 reconstruction [95] acceleration factor 2 along the phase-encoding direction was used to minimize
883 image distortions and yield optimal BOLD sensitivity. The dummy volumes necessary to reach steady
884 state and the GRAPPA reconstruction kernel were acquired prior to the acquisition of the image data as
885 described in Lutti et al. [94]. Correction of the distortions in the EPI images was implemented using B0-
886 field maps obtained from double-echo FLASH acquisitions (matrix size 64x64; 64 slices; spatial resolution
887 $3mm^3$; short TE=10 ms; long TE=12.46 ms; TR=1020 ms) and processed using the FieldMap toolbox
888 available in SPM [96].
889
890 ***MRI data preprocessing***
891 fMRI data were analysed using SPM12 (www.fil.ion.ucl.ac.uk/spm). All images were first bias corrected
892 to compensate for image inhomogeneity associated with the 32 channel head coil [97]. Fieldmaps
893 collected during the scan were used to generate voxel displacement maps. EPIs for each of the twelve
894 sessions were then realigned to the first image and unwarped using the voxel displacement maps
895 calculated above. The three high-resolution structural images were averaged to reduce noise, and co-
896 registered to the whole brain structural scan. EPIs were also co-registered to the whole brain structural
897 scan. Manual segmentation of the vmPFC was performed using ITK-SNAP on the group averaged
898 structural scan normalised to MNI space. The normalised group mask was warped back into each
899 participant's native space using the inverse deformation field generated by individual participant
900 structural scan segmentations. The overlapping voxels between this participant-specific vmPFC mask and
901 the grey matter mask generated by the structural scan segmentation were used to create a native-space
902 grey matter vmPFC mask for each individual participant.
903
904
905

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Representational Similarity Analysis

Functional data were analysed at the single subject level without warping or smoothing. Each recall trial was modelled as a separate GLM, which comprised the 12 second period from the offset of the memory cue to just before the white flash which indicated to the participant they should open their eyes. Motion parameters were included as regressors of no interest. RSA [56], was performed using the RSA toolbox (http://www.mrc-cbu.cam.ac.uk/methods-and-resources/toolboxes/) and custom MATLAB (version R2014a) scripts. In order to account for the varying levels of noise across voxels which can affect the results of multivariate fMRI analyses, multivariate noise normalisation [98] was performed on the estimated pattern of neural activity separately for each trial. This approach normalises the estimated beta weight of each voxel using the residuals of the first-level GLM and the covariance structure of this noise. This results in the down-weighting of noisier voxels and a more accurate estimate of the task-related activity of each voxel.

The average number of voxels analysed in the vmPFC across the two sets of memories was 5252 (SD 1227). Whole ROI-based analysis was preferred to a searchlight approach which would involve comparing neural with model similarity matrices [99], as we did not have strong *a priori* hypothesis about changes in neural representations over time against which to test the neural data, nor did we want to make assumptions regarding the spatial distribution of informative voxels in the vmPFC.

As participants recalled two memories per time-point, the dataset was first split into two sets of eight time points, which were analysed separately using RSA. To characterise the strength of memory representations in the vmPFC, the similarity of neural patterns across recall trials of the same memory was first calculated using the Pearson product-moment correlation coefficient, resulting in a "within-memory" similarity score. Then the neural patterns of each memory were correlated with those of all other memories, yielding a "between-memory" similarity score. Both within- and between-memory correlations were performed on trials from separate runs. For each memory, the between-memory score was then subtracted from the within-memory score to provide a neural representation score (Fig 3C). This score was then averaged across the two memories at each time-point. Results for the left and

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the right hemispheres were highly similar, and therefore the data we report here are from the vmPFC bilaterally. A distinctive neural pattern associated with the recall of memories at each time period would yield a score significantly higher than zero, which was assessed using a one-sample t-test. Strengthening or weakening of memory representations as a function of remoteness would result in a significant difference in memory representation scores across time periods, and this was assessed using a one-way repeated measures ANOVA with post-hoc two-tailed paired t-tests. Error bars on graphs displaying neural representation scores were normalised to reflect within- rather than between-subject variability in absolute values, using the method recommended by Cousineau [100] for within-subjects designs. The range of values that we observed are entirely consistent with those in other studies employing a similar RSA approach in a variety of learning, memory and navigation tasks in a wide range of brain regions [101-110].

Searchlight analysis

An RSA searchlight analysis was conducted in normalised space, on multivariate noise-normalised data within the ROI. This approach selected every voxel within the ROI, and using a volumetric approach which is constrained by the shape of the ROI, expanded the area around that voxel until an area of 160 voxels was reached. Within each of these spheres, memories were correlated with themselves, and other memories, analogous to the standard ROI approach. Then the resulting neural RSM was correlated using Spearman's rank correlation coefficient with a model RSM which consisted of ones along the diagonal and zeros on the off-diagonal. This model RSM was used to detect if individual memories were detectable across all time-points. For every voxel, the average correlation from every sphere it participated in was calculated, to generate a more representative score of its informational content. Parametric assumptions regarding the spatial distribution of unsmoothed data may not hold. Therefore we used statistical nonparametric mapping (SnPM13) on the resulting searchlight images. We used 10,000 random permutations, a voxel-level significance threshold of t=3, and a family-wise-error corrected cluster-wise threshold of $p<0.05$ within an ROI.

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Experiment 2

Participants

Sixteen of the 30 participants who took part in Experiment 1 returned to take part in Experiment 2 (14 female, mean age 24.7, SD 3.1, range 21-33) approximately eight months later (8.4 months, SD 1.2).

Memory interview

Participants were presented with the 16 photographs and cue phrases associated with the autobiographical memories in Experiment 1 and were asked to describe in as much detail as possible the specific event which they had recalled previously. General probes were given by the interviewer where appropriate (e.g. "what else can you remember about this event?"). The interviewer availed of summarised transcripts from Experiment 1 to verify the same memory and details were being recalled. Participants then rated each memory on the same characteristics assessed in Experiment 1. The memory interview during Experiment 2 was also recorded and transcribed.

Behavioural analyses

The analysis of subjective and objective ratings for Experiment 2 followed exactly the same procedure as Experiment 1. The extent to which subjective ratings for the same memory had changed between Experiment 1 and Experiment 2 was assessed using a two-way (experiment x time period) repeated measures ANOVA with Bonferroni-corrected paired t-tests. Differences in objective memory ratings across experiments were analysed using a two (experiment) x two (detail) x eight (time period) repeated measures ANOVA with Bonferroni-corrected paired t-tests.

Task during fMRI scanning

Participants returned approximately one week later for the fMRI scan (mean 5.5 days, SD 3.7). Prior to scanning, only one reminder training trial per memory was deemed necessary given the prior experience

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of performing the task in Experiment 1. The scanning task remained unchanged from Experiment 1, aside from the re-randomisation of trials within each session. When the least vivid trials were excluded, the mean number of trials (/6) selected for analysis from each time period were as follows: 8M: 5.94 (SD 0.25), 12M: 5.97 (SD 0.13), 16M: 5.88 (SD 0.29), 20M: 5.88 (SD 0.29), 24M: 5.94 (SD 0.25), 28M: 5.94 (SD 0.17), 32M: 5.84 (SD 0.40), 68M: 5.81 (SD 0.36).

MRI data acquisition

Structural and functional data were acquired using the same scanner and scanning sequences as Experiment 1. However the prior acquisition of the partial volume structural MRI scans negated the need to include these in the protocol of Experiment 2.

MRI data preprocessing

fMRI data were preprocessed using the same pipeline as Experiment 1, with the additional step of co-registering the functional scans of Experiment 2 to the structural scans of Experiment 1, which enabled the use of the vmPFC masks from Experiment 1. First-level GLMs of each recall trial were constructed in an identical manner to Experiment 1.

Representational Similarity Analysis

RSA of the Experiment 2 fMRI data was conducted in an identical manner to Experiment 1. The average number of voxels analysed in the vmPFC across the two sets of memories for all participants was 5228 (SD 1765). To ascertain whether the observed neural representation scores had changed between Experiments 1 and 2, a two-way (experiment x time period) repeated measures ANOVA was performed. To investigate if these changes mirrored the predictions generated by the original data, paired t-tests were performed between the neural representation scores for each memory from Experiment 1 and Experiment 2, one-tailed if there was a hypothesised increase or decrease.

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Supporting Information

S1 Table. **Behavioural data for Experiment 1 (mean, SD) - Experiment 1 (n=30).**

A. Subjective ratings	0.5M	4M	8M	12M	16M	20M	24M	60M
Vividness	4.53 (0.52)	4.28 (0.55)	4.22 (0.50)	4.05 (0.53)	4.25 (0.50)	4.10 (0.50)	4.10 (0.52)	4.13 (0.67)
Detail	4.38 (0.54)	3.88 (0.61)	3.93 (0.49)	3.67 (0.75)	3.80 (0.60)	3.68 (0.71)	3.80 (0.57)	3.77 (0.78)
Effort	1.25 (0.39)	1.53 (0.45)	1.52 (0.50)	1.87 (0.57)	1.72 (0.47)	1.58 (0.44)	1.57 (0.49)	1.77 (0.57)
Personal significance	3.45 (0.88)	3.47 (0.75)	3.62 (0.80)	3.13 (0.85)	3.10 (0.93)	3.25 (0.98)	3.32 (0.72)	3.43 (0.83)
Valence	4.60 (0.46)	4.47 (0.51)	4.58 (0.47)	4.38 (0.60)	4.37 (0.57)	4.33 (0.44)	4.33 (0.50)	4.45 (0.58)
Active(1)/static event(2)	1.20 (0.25)	1.25 (0.31)	1.22 (0.31)	1.20 (0.28)	1.18 (0.31)	1.30 (0.39)	1.25 (0.34)	1.37 (0.37)
Self(1)/other perspective(2)	1.03 (0.13)	1.17 (0.36)	1.13 (0.29)	1.12 (0.25)	1.08 (0.19)	1.10 (0.24)	1.10 (0.20)	1.08 (0.27)
Recall frequency	3.23 (0.63)	2.78 (0.61)	2.95 (0.66)	2.55 (0.70)	2.72 (0.61)	2.88 (0.69)	2.63 (0.66)	2.83 (0.65)
Consistency	4.28 (0.49)	4.08 (0.76)	3.83 (0.75)	3.93 (0.54)	4.02 (0.65)	3.98 (0.53)	3.85 (0.71)	3.73 (0.69)
B. Objective scores								
Internal details	17.60 (5.42)	14.95 (3.95)	15.37 (5.96)	14.72 (6.75)	15.60 (4.84)	14.93 (5.74)	14.43 (3.89)	13.65 (4.50)
External details	6.35 (3.82)	6.03 (3.34)	6.38 (3.75)	6.08 (3.53)	5.82 (2.56)	6.02 (2.83)	5.78 (2.84)	6.07 (3.42)

S2 Table. **Neural representation scores (mean, SD) for other brain regions in Experiment 1 (n=30).**

Neural Representation	0.5M	4M	8M	12M	16M	20M	24M	60M
Precuneus	**.012 (.017)*** **	**.011 (.020)** **	**.015 (.013)*** **	**.013 (.012)*** **	**.011 (.015)*** **	**.013 (.014)*** **	**.016 (.018)*** **	**.016 (.017)*** **
Lateral temporal cortex	**.004 (.011)***	**.007 (.013)***	**.005 (.010)** **	**.007 (.012)** **	.003 (.009)	**.007 (.009)*** **	**.007 (.013)** **	**.007 (.011)*** **
Parahippocampal cortex	.004 (.011)	.003 (.011)	.005 (.013)	**.005 (.013)***	.003 (.013)	**.006 (.014)***	**.008 (.009)*** **	**.011 (.015)*** **
Retrosplenial cortex	.000 (.014)	.001 (.018)	.005 (.019)	.005 (.015)	**.006 (.015)***	.006 (.017)	.004 (.017)	**.008 (.017)***
Temporal pole	.003 (.009)	.002 (.012)	.003 (.012)	.003 (.009)	.001 (.010)	.002 (.009)	**.006 (.009)** **	**.008 (.008)*** **
Entorhinal/Perirhinal cortex	.002 (.012)	.004 (.013)	.000 (.012)	.002 (.011)	-.003 (.015)	.000 (.014)	.001 (.012)	**.006 (.013)***
Hippocampus	.001 (.007)	.000 (.010)	.002 (.011)	.003 (.010)	-.001 (.012)	.001 (.010)	.001 (.009)	**.004 (.008)** **

Asterisks indicate detectability from chance (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$).

S3 Table. **Behavioural data for Experiment 2 (mean, SD) - Experiment 2 (n=16).**

A. Subjective ratings	(0.5M) 8M	(4M) 12M	(8M) 16M	(12M) 20M	(16M) 24M	(20M) 28M	(24M) 32M	(60M) 68M
Vividness	3.47 (0.72)	3.41 (0.84)	3.34 (0.68)	3.19 (0.79)	3.09 (0.66)	3.31 (0.77)	3.22 (0.71)	3.09 (0.80)
Detail	3.22 (0.63)	3.25 (0.84)	3.13 (0.56)	2.84 (0.65)	3.06 (0.66)	3.09 (0.76)	2.97 (0.62)	2.75 (0.80)
Difficulty	2.34 (0.60)	2.19 (0.85)	2.22 (0.82)	2.28 (0.58)	2.25 (0.63)	2.22 (0.75)	2.28 (0.97)	2.25 (0.61)
Personal significance	2.97 (0.69)	3.13 (0.74)	3.22 (0.66)	2.78 (0.75)	2.84 (0.87)	2.94 (0.87)	2.66 (0.79)	3.00 (0.86)
Valence	4.31 (0.54)	4.28 (0.63)	4.28 (0.60)	4.06 (0.75)	4.22 (0.68)	4.03 (0.74)	3.97 (0.56)	4.38 (0.65)
Active(1)/static event(2)	1.31 (0.31)	1.41 (0.42)	1.38 (0.34)	1.47 (0.43)	1.19 (0.31)	1.34 (0.47)	1.34 (0.40)	1.28 (0.31)
Self(1)/other perspective(2)	1.09 (0.20)	1.13 (0.29)	1.13 (0.29)	1.16 (0.30)	1.00 (0.00)	1.06 (0.17)	1.16 (0.24)	1.09 (0.27)
Recall frequency	2.03 (0.69)	2.00 (0.80)	1.78 (0.75)	1.72 (0.45)	1.84 (0.77)	1.81 (0.70)	1.50 (0.48)	1.53 (0.59)
Consistency	3.94 (0.36)	3.94 (0.44)	3.91 (0.61)	3.88 (0.67)	3.91 (0.55)	4.00 (0.58)	3.81 (0.63)	3.72 (0.71)
B. Objective scores								
Internal details	18.75 (7.77)	17.56 (6.83)	17.59 (7.33)	18.66 (7.88)	19.63 (7.72)	20.31 (8.00)	17.06 (6.53)	16.03 (6.69)
External details	6.25 (4.27)	5.66 (4.06)	5.91 (2.78)	6.47 (4.46)	7.16 (3.34)	9.28 (5.40)	8.41 (5.18)	6.66 (4.36)

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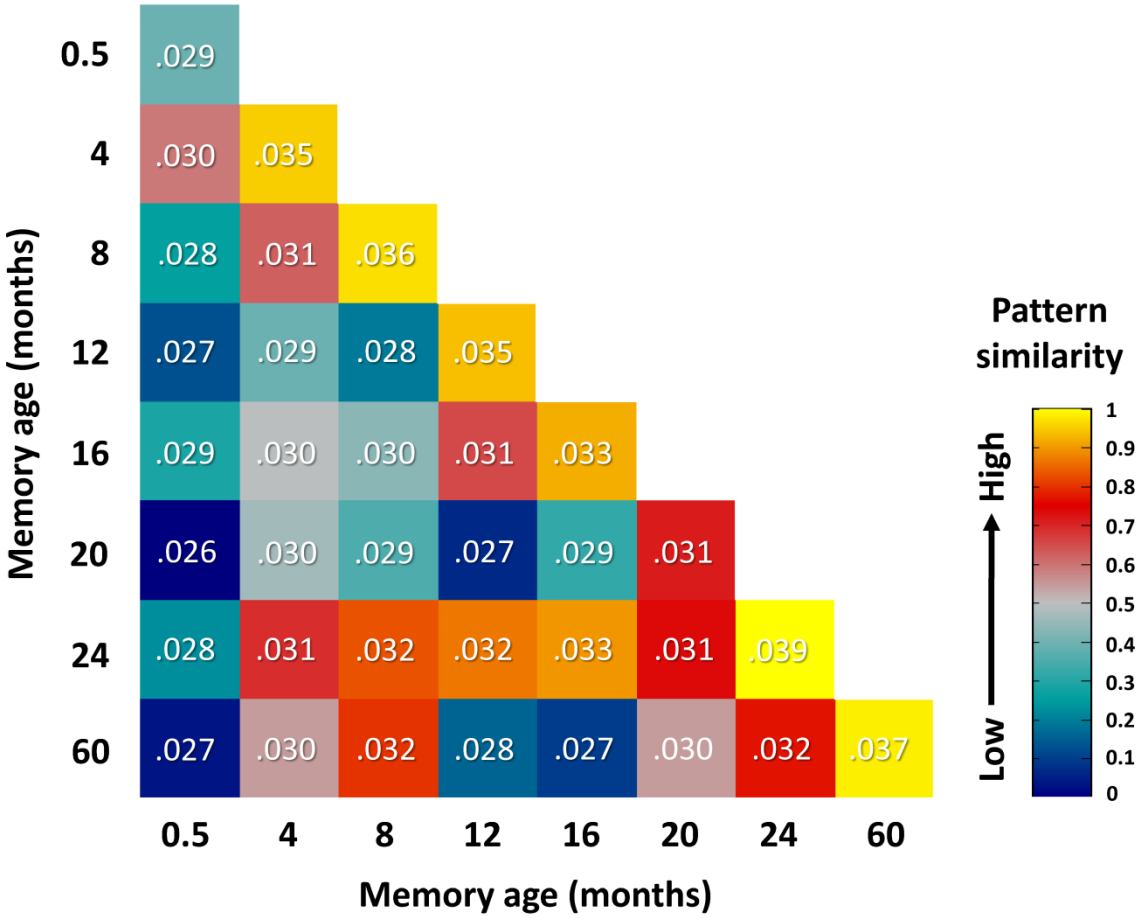

S1 Fig. Representational similarity matrix of within- and between time-point pattern similarity values for Experiment 1. Each cell in this matrix contains the group mean pattern similarity score between memories from all sampled time-points, averaged across the two memory sets. The values along the diagonal represent the within-memory similarity for each time-point. Off-diagonal values indicate the correlation of neural patterns between memories of different ages, which are subsequently averaged to produce the baseline "between-memory" value and subtracted from the "within-memory" correlation to produce a neural representation score. For ease of visual inspection, all values are rank transformed, scaled between zero and one and colour coded to indicate the magnitude of pattern similarity.

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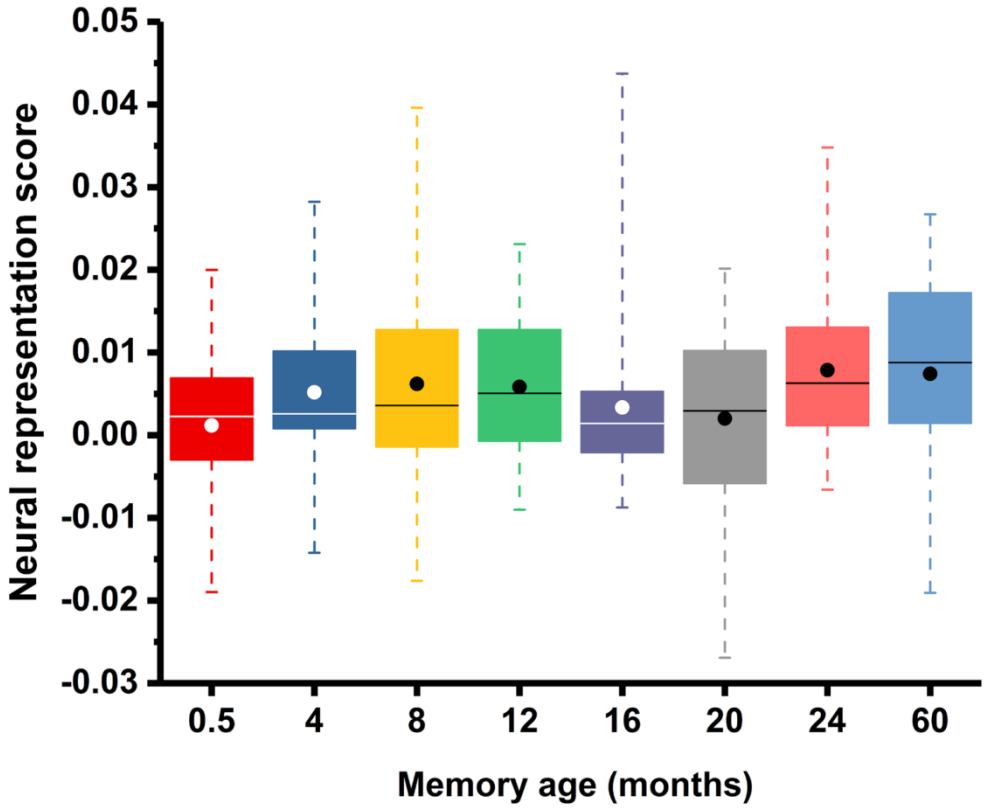

S2 Fig. Boxplot of neural representation scores for Experiment 1. Boxes represent 25th to 75th percentiles around the median; whiskers represent minimum and maximum values, means are indicated by solid circles (see S8 Data for individual participant numerical values).

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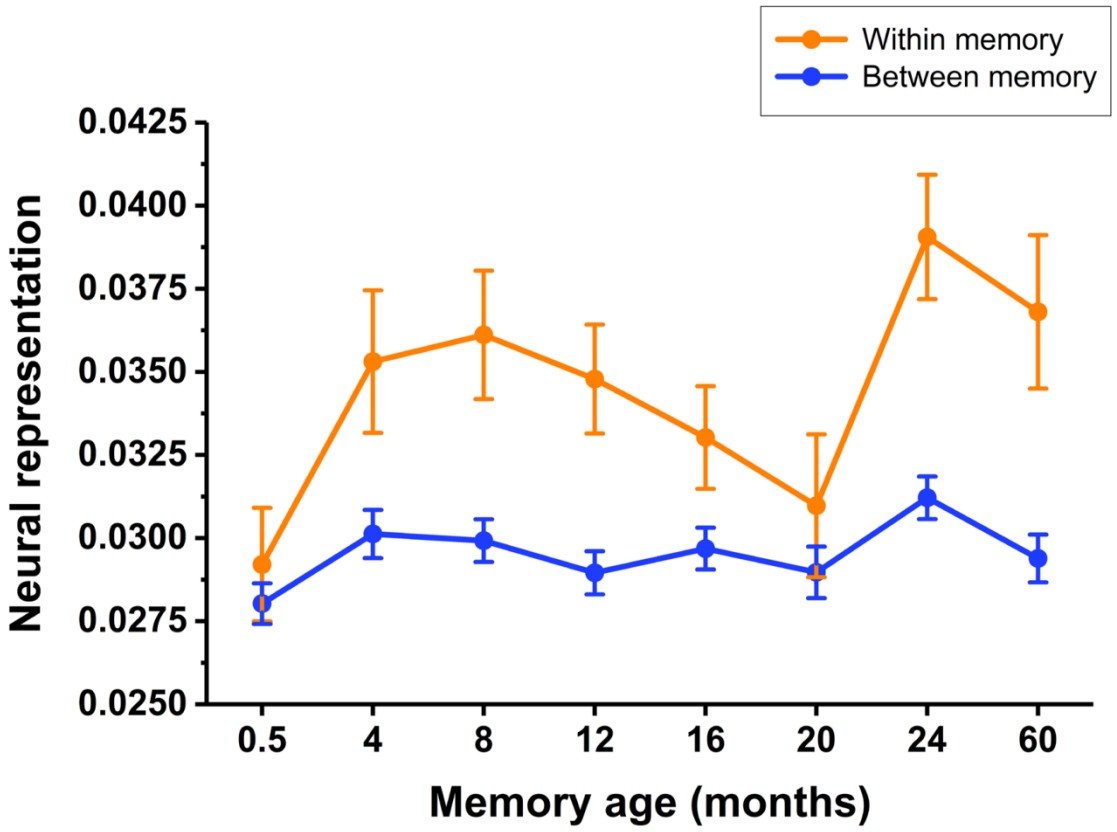

1309

1310 **S3 Fig. Within- versus between time-point pattern similarity for Experiment 1.** Time-dependent changes in neural
1311 representation scores were driven by within- rather than between-memory scores (see S9 Data for individual
1312 participant numerical values).
1313

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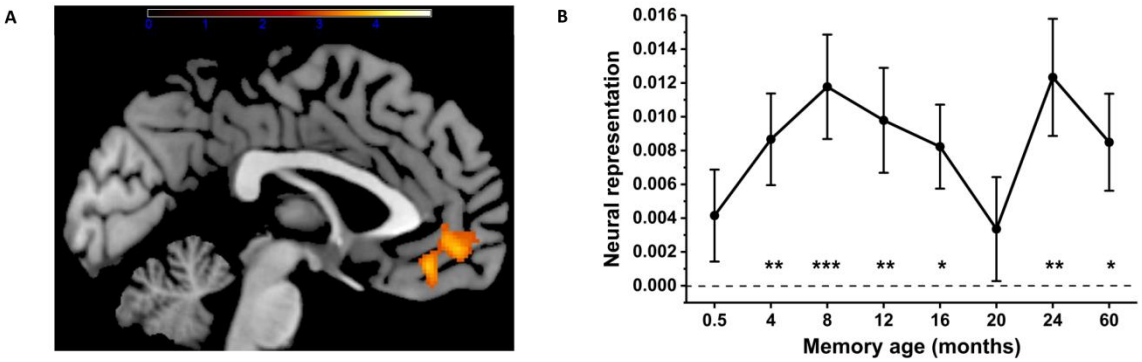

S4 Fig. Results of the group vmPFC searchlight analysis in MNI space for Experiment 1. (A) Colour-coded areas represent the FWE-corrected T-statistic where within-memory detectability was higher than between-memory detectability across participants. (B) Comparison of memory detectability across time-points within this functionally defined area, showing highly similar results to the whole ROI analysis in native space (see S10 Data for individual participant numerical values).