

Imagining the Future: Evidence for a Hippocampal Contribution to Constructive Processing

Brendan Gaesser,^{1*} R. Nathan Spreng,² Victoria C. McLelland,³
Donna Rose Addis,³ and Daniel L. Schacter¹

ABSTRACT: Imagining future events and remembering past events rely on a common core network, but several regions within this network—including the hippocampus—show increased activity for imagining future events compared to remembering past events. It remains unclear whether this hippocampal activity reflects processes related to the demands of constructing details retrieved across disparate episodic memories into coherent imaginary events, encoding these events into memory, novelty detection, or some combination of these processes. We manipulated the degree of constructive processing by comparing activity associated with the initial construction of an imagined scenario with the re-construction of an imagined scenario (imagine vs. re-imagine). After accounting for effects of novelty and subsequent memory, we found that a region in the hippocampus was preferentially activated for newly constructed imagined events compared with re-imagined events. Our results suggest that the hippocampus may support several distinct but related processes that are critical for imagining future events, and they also indicate that a particular region within posterior hippocampus may uniquely contribute to the construction of imagined future events. © 2013 Wiley Periodicals, Inc.

KEY WORDS: autobiographical; episodic memory; imagination; simulation; fMRI

INTRODUCTION

The capacity to imagine possible future events supports humans' ability to plan and prepare for new experiences in an adaptive manner. Whether preparing for a job interview, hunting for a new apartment, or anticipating a first date, mentally projecting ourselves into novel situations and simulating the potential consequences of different actions can help guide future decision-making (Buckner & Carroll, 2007; Gilbert & Wilson, 2007; Schacter & Addis, 2007; Schacter, 2012; Schacter et al., 2012). Considerable evidence indicates that imagining future events and remembering past events rely on a common core network that includes

the hippocampus in addition to other medial temporal, parietal, and prefrontal regions (for review, see Schacter et al., 2012). However, the role of the hippocampus in imagining future experiences has recently been the subject of debate.

Neuroimaging studies have consistently found evidence for hippocampal activation when people imagine future events (for review, see Addis & Schacter, 2012; Schacter et al., 2012). Indeed, several studies have shown that activity in the hippocampus is *greater* for imagining compared to remembering (e.g. Addis et al., 2007; Weiler et al., 2010; Addis et al., 2011). It has been suggested that such activity reflects more intensive constructive processing during imagining than remembering, that is, the hippocampus may play a role in recombining details gleaned from disparate episodic memories into a coherent novel scenario (Schacter & Addis, 2007). Evidence consistent with the idea that hippocampal activity is associated with a recombination process comes from studies that have observed greater hippocampal activity when the degree of constructive processing is increased by manipulating the probability that the event will occur (i.e. greater hippocampal activation for low than high probability future events; Weiler et al., 2010), the amount of recombined detail (Addis & Schacter, 2008) or the specificity of an imagined episode (Addis et al., 2011). Moreover, given the role of the hippocampus in relational processing and binding together disparate episodic details in working and long-term memory, this region seems well positioned to support a recombinatory process for imagining episodic experiences (Eichenbaum, 2001; Hannula et al., 2006; Hannula & Ranganath, 2008; Axmacher et al., 2010).

However, other findings call into question the possibility that the hippocampus plays a role in recombining details during the construction of imagined events. For example, hippocampal activity in neuroimaging studies is not always greater for imagined than remembered events; comparable levels of activity have been observed in some studies and greater hippocampal activity for remembering than imagining in others (for review and discussion, see Addis & Schacter, 2012; Schacter et al., 2012). Moreover, recent neuroimaging evidence reveals a role for the hippocampus in the successful encoding of imagined future events into episodic memory (Martin et al., 2011), raising the possibility that evidence for

¹Department of Psychology, Harvard University, Cambridge, Massachusetts; ²Laboratory of Brain and Cognition, Department of Human Development, Cornell University, Ithaca, New York; ³School of Psychology and Centre for Brain Research, The University of Auckland, Auckland, New Zealand

Grant sponsor: National Institutes of Health; Grant number: MH060941.

*Correspondence to: Brendan Gaesser, Department of Psychology, Harvard University, 33 Kirkland St., Cambridge, MA 02138, USA. E-mail: mailto:bgaesser@wjh.harvard.edu

Accepted for publication 24 May 2013.

DOI 10.1002/hipo.22152

Published online 10 July 2013 in Wiley Online Library (wileyonlinelibrary.com).

greater hippocampal activation during imagining than remembering reflects encoding-related activity. Finally, several studies of amnesic patients with hippocampal damage show that such patients exhibit impaired abilities to imagine coherent scenes and future events (see also, Tulving, 1985; Hassabis et al., 2007; Andelman et al., 2010; Race et al., 2011; Romero & Moscovitch, 2012; Klein et al., 2002.), but others find no such impairments (Maguire et al., 2010; Squire et al., 2010; Hurley et al., 2011, Cooper et al., 2011).

Addis and Schacter (2012) suggested that these discrepant findings could be reconciled if different regions within the hippocampus support separate component processes underlying imagining and remembering. This multicomponent account proposes that the hippocampus contributes to distinct but related processes that support imagining future events, including retrieving episodic details, recombining those details into coherent scenarios, and encoding the newly formed scenarios into episodic memory. From this perspective, hippocampal activation in neuroimaging studies of episodic simulation could potentially reflect the contributions of any of the three component processes, depending on the extent to which experimental conditions draw on each component. In neuropsychological studies of patient populations, partial damage to the hippocampus may impair specific component processes while leaving others relatively intact, thereby giving rise to differential patterns of impairment. Although the multicomponent view cannot resolve all discrepancies in the literature, it seems clear that elucidating the precise contribution of the hippocampus to imagination and future thinking requires teasing apart these intertwined component processes in a rigorous and controlled manner.

To clarify the contributions of the hippocampus to imagining future events, we drew on experimental recombination (Addis et al., 2009), subsequent memory (Wagner et al., 1998), and task switching paradigms (Duncan et al., 2012). Participants imagined novel future events constructed from person, place, and object details taken from their own autobiographical memories. Subjects imagined some future events for the first time in the scanner, and re-imagined other events that they previously imagined the day before. Events imagined for the first time should elicit a greater recombination demand than re-imagining events because they require the initial integration of disparate details into an event. However, events imagined for the first time are also more novel than re-imagined events, making it difficult to determine whether differential hippocampal activity for imagined compared with re-imagined events reflects differences in recombination demand or differences in event novelty (van Mulukom et al., in press). To control for novelty differences between imagine and re-imagine conditions, recombined person, place, and object detail sets were observed in a pre-exposure session the day before scanning in which subjects imagined future events for some of these detail sets, and judged the relative pleasantness of the details for others. Thus, the novelty of the event details was held constant across these two conditions by virtue of equivalent pre-exposure to the detail sets, but the details were

integrated into a coherent future event in the imagine condition and were not integrated into a coherent event in the pleasantness condition. In the scanner, trials involved either switching tasks using the same detail sets as the previous day or repeating the imagining task. Thus, subjects (1) imagined future events for the first time using detail sets for which they had previously judged pleasantness, (2) judged the pleasantness of person, place, and object details for the first time using some of the detail sets for which they had previously imagined an event, or (3) re-imagined events using the remaining detail sets that they had previously imagined the day before. After scanning, participants completed a cued-recall test, thus allowing us to hold constant encoding success for imagined and re-imagined events. If the involvement of the hippocampus in constructing imagined future episodes includes a recombination process, then we would predict greater hippocampal activity for imagined compared to re-imagined events after controlling for both encoding- and novelty-related processing.

MATERIALS AND METHODS

Participants

Twenty-four, right-handed healthy adults (16 females; age $M = 21.4$, $SD = 2.9$) with no prior history of psychiatric, neurological, or other medical impairment that could compromise cognitive function, and possessing normal or corrected-to-normal vision participated in this study. An additional nine participants were run but excluded from data analysis due to failure to produce enough successfully encoded trials (>10 per successfully remembered condition), task noncompliance, or excessive movement. All participants provided written informed consent and were compensated for their participation according to ethical guidelines approved by the Harvard University Institutional Review Board.

Materials and Procedure

Design

Subjects performed three main tasks of interest while in the scanner. They imagined future events for the first time using detail sets for which they had previously judged the relative pleasantness of details (*Imagine* condition), judged the relative pleasantness of details for the first time using some of the detail sets for which they had previously imagined an event (*Pleasant* condition), or re-imagined events using the remaining detail sets that they had previously imagined the day before (*Re-imagine* condition). Critically, both the *Imagine* and *Re-imagine* conditions consisted of detail sets that were retrieved from disparate episodic memories, but in the *Imagine* condition the details had previously been encountered during the pleasantness task, which did not require combining the details into a coherent episodic scenario, whereas in the *Re-imagine* condition, subjects had previously combined the details into a

coherent episodic scenario. All conditions are matched for prior exposure to the person-location-object triplets.

Pre-scan: Autobiographical memory collection

Approximately 1 week ($M = 10.3$ days, $SD = 3.0$) prior to scanning, participants came into the laboratory and recalled 200 autobiographical memories from the past 15 years, writing a description for every memory. Participants were allowed access to Facebook and were provided with a sample list of common life events to facilitate retrieval of the required number of memories. Each memory had to be specific in time and place (i.e. episodic) and comprised of a unique person, location, and object that could not be duplicated across events. The experimenter checked on the participant about once every hour to review the participant's progress and to ensure that the reported memories complied with instructions. Any reported memories that failed to comply with instructions were not used as stimuli in subsequent sessions. Before returning for the next session, person, location, and object details were recombined across memories, thereby creating 180 newly formed person-location-object sets that were derived from three separate autobiographical memories.

Pre-scan: Pre-exposure

The day prior to scanning, participants imagined future events involving 120 of these detail sets, and judged the relative pleasantness of the details for the remaining 60 sets. For the 120 imagined future event trials, participants silently imagined a specific novel event integrating the three details within a person-location-object set that could plausibly occur in next 5 years. For the 60 pleasantness trials, participants constructed a sentence ranking the relative pleasantness of details within a person-location-object set, "Wedding ring is more pleasant than JFK Park is more pleasant than Sally", for example. Participants were given 9 s to imagine an event or rank the pleasantness of details. Following these tasks, participants provided a unique title that briefly summarized a generated event or judgment (e.g. "Playing badminton with Adrian" for an imagined trial, "Wedding ring > JFK Park > Sally" for a pleasantness trial).

Scanning

Immediately before entering the scanner, participants were administered practice trials (one trial for each condition) and the experimenter ensured that all instructions were understood. In the scanner, trials consisted of either switching task conditions (judging the relative pleasantness of person-location-object details that were used to imagine future events during the pre-exposure session or vice versa) or repeating the imagining task using the same person-location-object detail sets as in the pre-exposure session (see Fig. 1). For 9 s, task instruction prompts were presented along with person-location-object detail sets and event or judgment titles that participants generated the previous day. Presenting titles during scanning that summarize previously generated events or judgments holds

constant differences that might reflect repeating or recalling experiences from the pre-exposure session; varying across conditions is whether or not disparate details have been recombined into a specific imagined episode.

The experimental design yielded these three condition types (*Imagine, Pleasant, Re-imagine*) composed of 60 trials each labeled according to the task completed during scanning. Participants also completed 30 trials of size judgment task (*Size* condition) based on a previous study by Addis et al. (2009), during which they had 9 s to integrate three nouns into a sentence that ranked the relative size of each item in a "X is bigger than Y is bigger than Z" format. Phenomenological ratings of how detailed the imagined event was (for *Imagine* and *Re-imagine* trials) or how difficult it was to make a relative judgment (for *Pleasantness* and *Size* trials) were collected using a button box (1 = low, 4 = high) for 3 s following imagining an event or making a relative judgment. These phenomenological ratings (i.e. detail and difficulty) not only offer information concerning subjective experiences, but also serve as an online indicator of task compliance in the scanner on a trial-by-trial basis, hence subsequent analyses only include trials during which participants provided a response. Notably, participants provided a response for 95% of trials, indicating a high rate of task compliance. Each trial (experimental task + phenomenological rating; 12 s) was randomly interleaved with 3, 6, or 9 s of fixation, allowing for an event-related analysis by establishing temporal jitter in the experimental design.

Post-scanning: Subsequent memory test

Ten minutes after the last experimental trial, participants completed a surprise cued-recall task using a procedure similar to that used in previous studies for testing memory of events with several elements (Jones, 1976; Martin et al., 2011; Szpunar et al., 2012). The test was composed of 180 trials, 60 trials each from the *Re-imagine*, *Imagine*, and *Pleasant* tasks presented during scanning. On every trial of the memory test, two of three details (person and place, place and object, or person and object) from a scanning trial were presented and the missing detail was to be recalled. Since participants were instructed during scanning to integrate all three details—either into a coherent event (*Imagine* and *Re-imagine*), or by making a relative judgment (*Pleasant*)—subsequent memory for these details reflects how well these details were bound together. The detail to be recalled was counterbalanced across detail type (person, location, or object). Participants were instructed that they could guess if they felt reasonably certain of the right answer. The test was self-paced, lasting about 1 hour.

fMRI parameters and preprocessing

Brain imaging data were collected on a 3T Siemens Magnetom Tim Trio MRI scanner with a 12-channel phased-array whole-head coil. Anatomical scans were acquired using a T1-weighted high-resolution three-dimensional magnetization-prepared rapid gradient echo sequence (MPRAGE; 176 sagittal

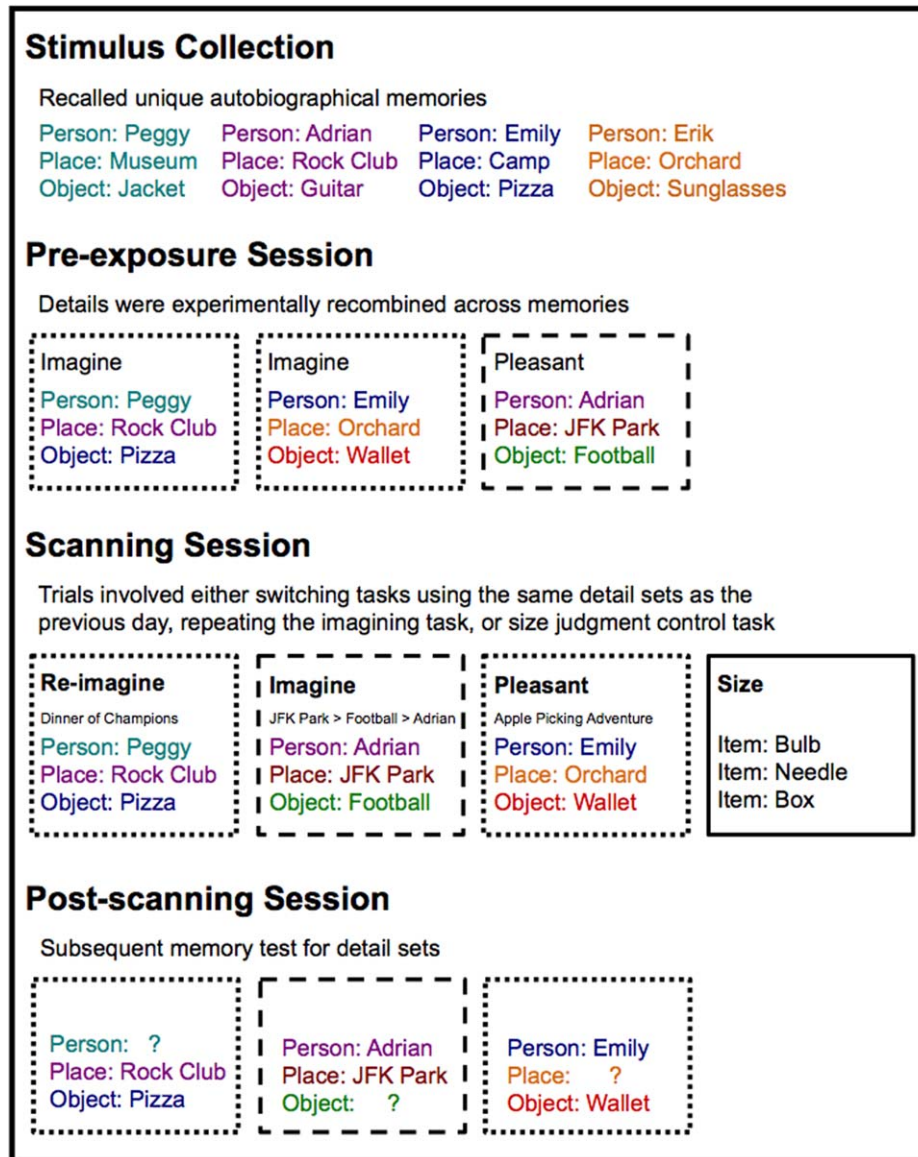


FIGURE 1. The study involved four experimental sessions. First, participants recalled autobiographical memories. Second, participants imagined events or made pleasantness judgments on detail-sets experimentally recombined across autobiographical memories. Third, participants re-imagined the same event from the

previous session, imagined an event for the first time, made pleasantness judgements for the first time, or completed a size judgment control task. Finally, subsequent memory performance was assessed with cued-recall test. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

slices, TR = 2530 ms, TE = 1.64 ms, 7° flip angle, 1 mm isotropic voxels). Six task blood-oxygen-level-dependent (BOLD) functional scans were acquired using a T2*-weighted echo-planar imaging (EPI) pulse sequence (47 interleaved axial slices parallel to the anterior-posterior commissure plane, TR = 3000 ms, TE = 30 ms, 85° flip angle, no skip between slices, 3 mm isotropic voxels). Task stimuli were presented using E-Prime software to display text that was projected onto a screen at the head of the scanner and reflected into a mirror on top of the head coil for the participant to see. Two additional 6 min 12 s resting state BOLD scans (not presented

here) were acquired at the beginning and end of the scanning session. Cushions were used to minimize head movement during scanning. Participants made responses using a button box placed in their right hand.

Functional scans were preprocessed using SPM2 (Wellcome Department of Cognitive Neurology, London, UK). To allow for T₁-saturation effects, the initial four volumes in each run were excluded from analyses. Data were corrected for slice-dependent timing differences and for head movement within and across runs using a rigid body correction. Data were then spatially normalized to the standard space of the Montreal

Neurological Institute (MNI) atlas (resampled at 2 mm cubic voxels), and spatially smoothed with a 6 mm full-width half-maximum Gaussian kernel. All coordinates are reported in MNI space.

After preprocessing, data were analyzed with the general linear model using SPM8. The BOLD responses for seven trial types (i.e. imagine hit, imagine miss, re-imagine hit, re-imagine miss, pleasant hit, pleasant miss, size sentence) were modeled for each participant. The onsets of these trials were then convolved with the canonical hemodynamic response function to create regressors of interest. In doing so we restricted our analyses to the neural activity related to the construction phase of simulating events and thereby minimize contamination by other cognitive processes including elaboration-related activity, consistent with previous methods (Addis et al., 2007; Martin et al., 2011). Additional covariates of no interest (a session mean, a linear trend, and subject-specific movement parameters) were also modeled. First-level planned contrasts (i.e. fixed effects models) were performed on these parameter estimates, and contrast images for each participant were subsequently entered into a second-level analysis treating participants as random effects. For the imagine and re-imagine conditions, linear parametric modulation regressors of detail ratings were included to (1) ensure that differences between conditions are not simply attributed to the amount of details retrieved and (2) account for known detail modulation effects in the hippocampus (Addis & Schacter, 2008; Martin et al., 2011).

Contrasts of interest were run in order to identify regions preferentially engaged by: (1) imagining future events by comparing imagined future events relative to the semantic control task (i.e. *Re-imagine* + *Imagine* > *Size*); and (2) constructing novel future events by comparing initial simulations with repeated simulations (i.e. *Imagine* > *Re-imagine*). The two analyses were confined to successfully remembered trials, allowing us to hold constant encoding-related activity (i.e. *Imagine* > *Re-imagine*, for hits only). However, as noted in the Introduction, a simple comparison of Imagine and Re-imagine conditions does not allow us to distinguish constructive activity or recombination demand on the one hand, and event novelty on the other. To remove activity related to novelty, we performed an additional analysis in which we subtracted activity from the *Pleasant* condition (i.e. [*Imagine* > *Pleasant*] > [*Re-imagine* > *Pleasant*]). As noted earlier, this condition controls for novelty because, just like in the Re-imagine condition, it elicits activity related to the retrieval of disparate details across episodic memories, but unlike in the Re-imagine condition, these details must be recombined or integrated for the first time into a coherent imagined scenario. Thus, we computed the following contrast to control for activity related to both encoding and novelty (i.e. [*Imagine* > *Pleasant*] > [*Re-imagine* > *Pleasant*], for hits only).

The minimum cluster size required for corrected significance was calculated using the 3dClustSim (an adaptation of AlphaSim) AFNI program, which estimates the overall probability of false positives within a search volume through a Monte Carlo simulation (10,000 iterations). For whole-brain contrasts, we

report all activations at a voxel-level threshold of $P = 0.001$ combined with a spatial extent threshold of 89 voxels, yielding a threshold of $P < 0.05$ corrected for multiple comparisons. Since the hippocampus was an a priori region of interest, we calculated a corrected threshold using a bilateral hippocampal volume (1878 2mm³ voxels), setting a $P < 0.05$ threshold with a $P = 0.005$ voxel-level threshold and extent threshold of 18 voxels (Yassa & Stark, 2008).

RESULTS

Behavioral Results

Behavioral data confirmed participant compliance during scanning as well as in the post-scan session. Comparisons were performed using a paired-samples *t*-test or repeated measures ANOVA (Bonferroni correction for multiple comparisons, $\alpha < 0.05$), where appropriate. On a four-point Likert scale (1 = low detail, 4 = high detail), re-imagined future events were rated significantly more detailed ($M = 2.87$, $SE = 0.10$) than imagined future events ($M = 2.73$, $SE = 0.10$), $t(23) = 2.58$, $P < 0.05$ (see Table 1). In addition to ratings serving as an indicator of subject compliance on a trial-by-trial basis during scanning, this pattern of detail ratings suggests that during the pre-exposure session, participants were able to comply with task instructions to either discretely imagine an event, or to judge the pleasantness of details without constructing an imagined event during the pre-exposure phase: if subjects had imagined events during the pleasantness task, one would expect detail ratings to be similar across Imagine and Re-imagine conditions, but this was not the case. Subsequently-remembered imagined and re-imagined events (hits) were significantly more detailed ($M = 3.01$, $SE = 0.08$) than subsequently forgotten imagined and re-imagined events (misses; $M = 2.59$, $SE = 0.10$), $t(23) = 7.88$, $P < 0.001$. Although detail ratings significantly differed across Imagine and Re-imagine conditions and predicted subsequent memory performance, since detail ratings were included in SPM as parametric modulator, any changes in BOLD signal associated with detail would be accounted for in our model.

TABLE 1.

Behavioral Results

| Subsequent memory | Imagine | Re-imagine | Pleasant |
|-------------------|-----------------------------|--------------|--------------|
| | Mean detail rating (and SE) | | |
| Hit | 2.94 (.08) | 3.08 (.08) | |
| Miss | 2.51 (.01) | 2.66 (.09) | |
| Hit and miss | 2.73 (.01) | 2.87 (.01) | |
| | Mean # of trials (and SE) | | |
| Hit | 27.45 (2.37) | 44.71 (1.51) | 22.45 (1.62) |
| Miss | 28.83 (2.23) | 12.17(1.35) | 35.17(1.79) |
| Hit and miss | 56.29 (1.08) | 56.89 (0.81) | 57.63(1.13) |

To evaluate subsequent memory differences across experimental tasks, we compared difference scores (subtracting the number of misses from the number of hits) for each experimental task. The difference scores were as follows: Re-imagine ($M = 32.54$, $SE = 2.74$), Imagine ($M = -1.38$, $SE = 4.48$), Pleasantness ($M = -12.70$, $SE = 3.21$). The number of hits compared to misses systematically varied across conditions [$F(2,46) = 95.20$, $P < 0.001$]. Re-imagine trials were more likely to be subsequently remembered than Imagine and Pleasant trials. Further, Imagine trials were more likely to be remembered than Pleasant trials. Although one must be cautious interpreting subsequent memory effects (i.e. hits compared to misses) from different bin sizes across conditions to avoid confounding effects of experimental task with subsequent memory, these observed differences should not systematically bias interpreting differences in BOLD signal across conditions restricted to subsequently remembered items only.

fMRI Results

Imagining future events

Imagination conditions, relative to the semantic control task (i.e. Imagine + Re-imagine > Size), revealed activation in medial prefrontal cortex, posterior cingulate cortex, retrosplenial cortex, middle frontal gyrus, lateral and medial temporal lobes, consistent with many previous studies (for review, Schacter et al., 2012) (see Table 2, Fig. 2A).

Encoding and novelty in the hippocampus

To examine novelty processing, we contrasted conditions that involved switching tasks across sessions to the condition that repeats the same task (Pleasant + Imagine > Re-Imagine). This contrast showed significant activity in regions (-22, -26, -8; 22, -28, -6) near the midline of the long axis of hippocampus extending anteriorly, similar to previous observations (e.g. Kumaran & Maguire, 2007).

To examine encoding effects, we contrasted hits versus misses collapsed across Imagine and Re-imagine conditions. Consistent with Martin et al. (2011), we observed evidence that the anterior hippocampus supports encoding activity. Our analysis revealed a single cluster (-28, -6, -28) activated at a voxelwise threshold of $P = 0.012$ which when combined with a spatial extent of 21 voxels in 3dClustSim approached a corrected threshold of $P = 0.10$. While this hippocampal activity is only suggestive, most likely because we had far fewer trials than did Martin et al. (2011) due to design constraints of our study, the activity observed here generally aligns well with the findings of Martin et al. (2011).

Constructing future events: Hippocampal analysis

Contrasting activation engaged by imagining an event for the first time compared to re-imagining the same event (Imagine > Re-imagine) elicited greater activity in the right anterior and bilateral posterior hippocampus. This contrast revealed candidate regions that could support a constructive process, since imagining an event for the first time requires the initial

TABLE 2. *fMRI Results: Whole-Brain*

| Brain region | Peak MNI coordinate (x, y, z) | Z-score |
|--|-------------------------------|---------|
| <i>Re-imagine + Imagine < Size Control</i> | | |
| R posterior cingulate | 2, -56, 22 | 7.32 |
| L ventral mPFC | -8, 36, -14 | 6.66 |
| L middle temporal gyrus | -58, -6, -18 | 6.57 |
| R middle temporal gyrus | 52, -6, -26 | 5.67 |
| R precuneus | 6, -56, 50 | 5.44 |
| L superior frontal gyrus | -20, 30, 46 | 5.33 |
| L superior frontal gyrus | -12, 54, 46 | 5.02 |
| R temporal pole | 40, 20, -38 | 4.82 |
| R middle frontal gyrus | 42, 14, 30 | 4.75 |
| R cerebellum | 14, -72, -30 | 4.23 |
| R cerebellum | 14, -88, -40 | 4.16 |
| R orbital frontal cortex | 30, 26, -24 | 3.99 |
| R superior frontal gyrus | 24, 26, 44 | 3.68 |
| <i>Imagine > Re-imagine</i> | | |
| L lateral occipital gyrus | -26, -88, 18 | 5.50 |
| R anterior precuneus | -6, -54, 50 | 4.89 |
| R fusiform gyrus | 24, -84, -6 | 4.72 |
| R fusiform gyrus | 30, -84, -6 | 4.72 |
| R superior frontal gyrus | 32, 20, 62 | 4.52 |
| L superior frontal gyrus | -26, 40, 42 | 4.42 |
| L inferior temporal gyrus | -38, -58, -4 | 4.33 |
| <i>(Imagine > Pleasant) > (Re-imagine > Pleasant) hits only</i> | | |
| R superior frontal gyrus | 24, 22, 56 | 4.77 |
| L lateral occipital gyrus | 24, -88, 20 | 4.67 |
| R superior parietal lobule | 20, -70, 56 | 4.64 |
| L fusiform gyrus | -26, -84, -4 | 4.38 |
| Calcarine cortex | 0, -90, 4 | 4.36 |
| L superior parietal lobule | -20, -62, 52 | 3.97 |
| <i>Re-imagine > Imagine, hits only</i> | | |
| L inferior frontal gyrus | -42, 28, -8 | 4.74 |
| L middle temporal gyrus | -48, -28, -10 | 4.27 |
| L angular gyrus | -40, -60, 44 | 4.20 |
| L posterior precuneus | -8, -70, 34 | 4.05 |

All activations are significant at a $P < 0.05$ threshold corrected for multiple comparisons with a $P = 0.001$ voxel-level threshold and extent threshold of 89 voxels. MNI, Montreal Neurological Institute; L, left; R, right.

construction of disparate details into an event rather than the less intensive processing of re-construction. However, as pointed out earlier, this contrast does not allow us to separate processes associated with construction of imagined events from those associated with novelty detection or encoding. To control for these confounds, we ran a tighter contrast that removed activity associated with novelty of event details (Pleasant condition) and held encoding constant by constraining our analysis to hits only (i.e. [Imagine > Pleasant] > [Re-imagine > Pleasant], for hits only). This more rigorous contrast revealed that only the left posterior hippocampus, distinct from regions implicated in encoding and novelty, remained preferentially engaged, (see Fig. 3, Table 3).

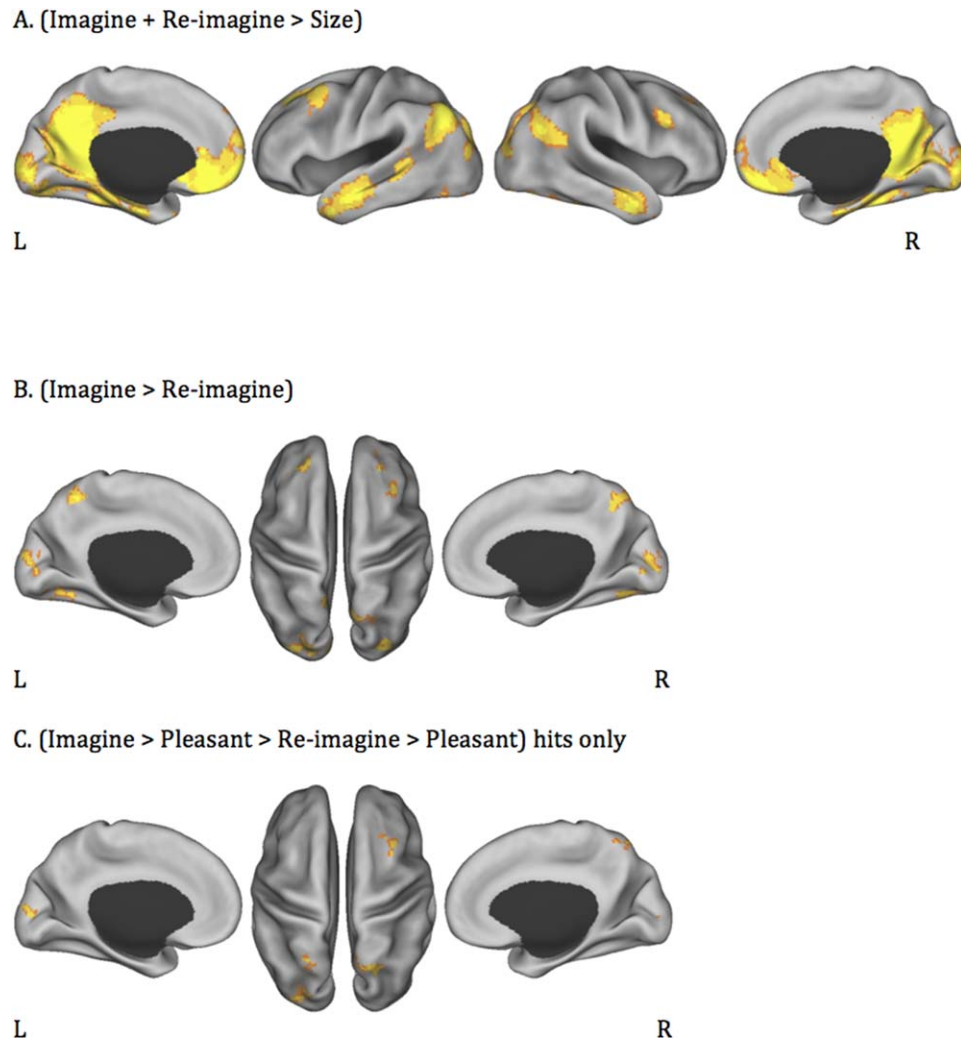


FIGURE 2. Whole-brain activations are significant at a $P < 0.05$ threshold corrected for multiple comparisons with a $P = 0.001$ voxel-level threshold and minimum extent threshold of 89 voxels. L, left; R, right. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Constructing future events: Whole brain analysis

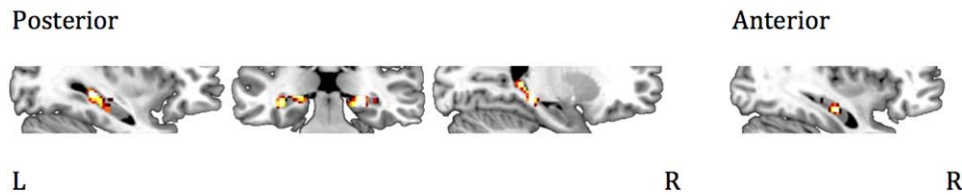
Contrasting activation during imagining an event for the first time compared to re-imagining the same event (Imagine > Re-imagine) revealed increased activity in the superior frontal gyri and regions in occipital and temporal cortex related to visual/imagery processing (see Table 2, Fig. 2B). We then controlled for novelty- and encoding-related activity by subtracting activity associated with the Pleasant condition and held subsequent memory performance constant (i.e. [Imagine > Pleasant] > [Re-imagine > Pleasant], for hits only). This contrast showed activity in bilateral parietal lobes as well as activity in regions related to visual/imagery processing, but now most prominently observed was activity in the right superior frontal gyrus (see Table 2, Fig. 2C). We also examined increases in activity for repeated simulations (Re-imagine > Imagine). This contrast revealed greater activity for re-imagining compared to

imagining in the superior precuneus, inferior frontal gyrus, and lateral temporal cortex (see Table 2).

DISCUSSION

A distributed network of brain regions that includes the hippocampus is commonly activated for remembering the past and imagining the future (Buckner & Carroll, 2007; Hassabis & Maguire, 2007; Schacter et al., 2007; Spreng et al., 2009; Schacter et al., 2012). Moreover, the hippocampus has also shown increased activity for imagining compared to remembering (e.g. Addis et al., 2007; Weiler et al., 2010; Addis et al., 2011). It has been proposed that this preferential hippocampal activity reflects the increased recombination demand associated with integrating disparate episodic details into coherent

A. (Imagine > Re-imagine)



B. (Imagine > Pleasant > Re-imagine > Pleasant) hits only

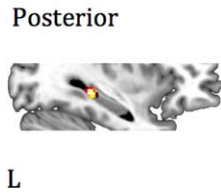


FIGURE 3. As the hippocampus was an a priori region of interest, activations are presented at a $P < 0.05$ threshold corrected for multiple comparisons with a $P = 0.005$ voxel-level threshold and extent threshold of 17 voxels with the whole brain masked to only show voxels within the bilateral hippocampus. L, left; R, right. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

scenarios (Schacter & Addis, 2007). The aim of the present study was to evaluate this hypothesis by examining whether hippocampal activity is sensitive to differences in constructive demand after controlling for both encoding- and novelty-related activity. Our findings suggest that the hippocampal contributions to imagining future events extend beyond encoding and novelty processing because even with these processes controlled for, left posterior hippocampus was involved in the constructive process of recombining disparate details from memory into a coherent scenario when simulating a future event.

Although previous studies have observed increased hippocampal activity under conditions that have been interpreted as reflecting a more intensive or demanding constructive processing (Addis & Schacter, 2008; Addis et al., 2007, 2011; Weiler et al., 2010), the confounding influences of encoding- and novelty-related processes have made this claim difficult to evaluate. Our results thus provide some support to previous interpretations of increased hippocampal activation during imagining compared with remembering as reflecting differences in recombination processing (e.g. Addis et al., 2007). Although a few studies have found that remembering past events evokes greater activity than imagining future events (Hassabis et al., 2007; Botzung et al., 2008; D'Argembeau et al., 2008), the paradigms used in these studies required subjects to pre-imagine events before being scanned, thereby reducing constructive demand during the scanning session. Thus, rather than offering contradictory findings, these studies suggest that the online construction of imagined events is an important feature to consider when interpreting existing results and designing future studies.

While the evidence for a constructive, recombinatory process in the hippocampus under the stringent conditions of the

present experiment provides support for the idea that the hippocampus plays a role in generating imagined events, the anterior–posterior localization of this activity conflicts with previous reports that the anterior hippocampus in particular underlies recombination (Addis et al., 2007; Schacter & Addis, 2009; Weiler et al., 2010). One possible explanation is that the anterior hippocampal activity in these studies reflects the encoding of novel episodes as opposed to their construction. Consistent with the anterior hippocampus reflecting the encoding of novel imagined events, Martin et al. (2011) showed that this region was more active for successfully remembered compared to successfully forgotten imagined future events constructed online in the scanner. They also observed a cluster in the posterior hippocampus that was greater for successfully remembered versus forgotten imagined events. However, in the

TABLE 3.

fMRI Results: Hippocampal Masked

| Brain region | Peak MNI coordinate (x, y, z) | Z-score |
|--|-------------------------------|---------|
| <i>Imagine > re-imagine</i> | | |
| Anterior right hippocampus | 36, -18, -14 | 3.25 |
| Posterior right hippocampus | 24, -28, -10 | 3.69 |
| Posterior left hippocampus | -36, -34, -6 | 3.69 |
| <i>(Imagine > pleasant) > (re-imagine > pleasant) hits only</i> | | |
| Posterior left hippocampus | -36, -36, -6 | 3.22 |

Activations are significant at a $P < 0.05$ threshold corrected for multiple comparisons with a $P = 0.005$ voxel-level threshold and extent threshold of 17 voxels. MNI, Montreal Neurological Institute; L, left; R, right.

absence of a manipulation that distinguishes encoding processes from recombination processes, it is difficult to tease apart a constructive process that requires the binding of details into a coherent event from processes that support the successful encoding of those details into an enduring memory trace.

Further evidence suggesting that the anterior hippocampus encodes novel episodes comes from a number of studies that demonstrate an encoding-retrieval distribution along the anterior-posterior axis of the hippocampus with the anterior supporting encoding and the posterior supporting retrieval (Lepage et al., 1998; Spaniol et al., 2009). Moreover, the anterior hippocampus appears particularly engaged when encoding associative information (Schacter & Wagner, 1999; Kirwan & Stark, 2004; Chua et al., 2007). However, we must be cautious about making strong claims exclusively linking the posterior hippocampus with recombination processes. For example, a recent meta-analysis of neuroimaging studies investigating medial temporal lobe activity during remembering and imagining tasks revealed that a number of parameters (i.e. type of cue, task, event specificity) can impact the precise location of activity in the hippocampus and related regions (Viard et al., 2012). Future studies capable of distinguishing constructive processing from encoding using a variety of such manipulations are needed before making strong claims.

Given the involvement of the posterior hippocampus in spatial processing (Maguire et al., 2000; Hassabis et al., 2007), it may be that this region supports the formation of a coherent spatiotemporal representation from disparate episodic details. Indeed, to the extent that simulations of future events meaningfully inform planning and preparation, this process seems critical. If the idea has merit, amnesic patients with posterior hippocampal damage should exhibit problems forming a coherent spatiotemporal imagined event, but as noted earlier the nature and even existence of imagination deficits in hippocampal amnesics is currently the topic of intensive debate (cf., Squire et al., 2010; Maguire & Hassabis, 2011; for review, see Addis & Schacter, 2012). Although most reported cases of hippocampal amnesic patients exhibiting an intact ability to construct imagined events have not included measures of event integration or spatial coherence (e.g. Squire et al., 2010), Maguire and Hassabis (2011) claim that the patients studied by Squire et al. (2010) appear to exhibit a reduction in spatial details relative to typical numbers generated by controls.

Evidence potentially relevant to our findings comes from Hassabis et al. (2007), who found that four of five amnesic subjects showed imagination deficits on their scene construction task. Nonetheless, they did observe one amnesic patient with a spared ability to vividly imagine events, PO1. PO1 suffered from dense amnesia, with 50% bilateral hippocampal volume loss, and a preserved ability to construct imagined scenarios—including unimpaired performance on measures of spatial coherence. This patient displayed signs of intact hippocampal tissue, raising the possibility that preserved ability to construct novel scenarios is dependent on residual hippocampal tissue. Using fMRI to scan PO1, Mullally et al. (2012)

observed two regions in the patient's medial temporal lobe that were more active for imagining coherent scenarios compared to imagining acontextual objects, the hippocampus (36, -28, -14) and the parahippocampus (33, -46, -5). Interestingly, the region we found to be associated with recombination in the present study is between these coordinates along the longitudinal axis. Of course, making inferences regarding the axis of the hippocampus across intact and severely atrophied hippocampi must be done with great caution, because the possibility of a potential functional reorganization induced by the lesion remains unknown.

The pattern of posterior hippocampus activity we observed in the present study also aligns nicely with ideas presented in a recent review of long-axis functional specialization in the hippocampus. In their review, Poppenk and colleagues (2013) proposed that differences in network connectivity and subfield composition better position the posterior hippocampus to represent fine-grained information compared with the anterior hippocampus, which preferentially represents more global features. From this perspective, imagining an event for the first time may require the initial construction of precise spatial and temporal details, whereas re-imagining the same event does not elicit the same degree of fine-grained construction. Further research is needed to directly test how these local and global functional specializations contribute to representations of imagined future events.

One limitation of our study is that while we infer a difference in the degree of constructive processing between imagining an event for the first time and re-imagining the same event, we did not collect independent measures of constructive processing across these tasks. One way for future research to overcome this limitation would be to collect difficulty ratings for all conditions (we collected difficulty ratings only for the Pleasant and Size conditions): more demanding constructive processing should elicit greater difficulty ratings compared with less intensive constructive processing.

Differences observed between imagining and re-imagining could also be attributed to differences resulting from some form of priming (i.e., the imagine condition could be conceived as an unprimed condition whereas the re-imagine condition could be conceived as a primed condition). However, recent studies examining future event simulation using a repetition suppression paradigm (van Mulukom et al., in press; Szpunar et al., in press), which measures effects similar to priming, did not report changes in posterior hippocampal activity, and therefore priming effects are unlikely to explain the difference between imagining and re-imagining observed here. However, these differences might be related to differences in encoding and/or retrieval. While we attempted to control encoding-related activity by matching subsequent memory performance of imagined details (i.e. person, place, or object sets), this procedure equates for encoding success; it is possible that imagining requires greater encoding effort than does re-imagining; conversely, re-imagining may require greater retrieval processing of the pre-exposure session than imagining does.

It is also worth noting that while the experimental design we used here controlled for the novelty of retrieving disparate episodic details (a requirement of both Imagine and Re-imagine), and task novelty (by contrasting Imagine and Re-imagine with the Pleasant condition), it does not rule out the possibility that our data reflect the influence of novelty-related processing attributable to imagining new events. Events constructed for the first time (Imagine) are novel compared to events constructed for the second time (Re-imagine). Thus, activity in the hippocampus that we interpret as reflecting constructive processing could also be attributable to *event* novelty. However, event novelty is an inherent property of event construction, so the two may be difficult to separate. Future research is needed to determine whether and to what extent it is possible to tease apart the close relationship between event novelty and construction of imagined future events.

Our results provide evidence that the hippocampus contributes to a constructive or recombinatory process that supports the ability to imagine future events. In light of other evidence that the hippocampus contributes to both encoding and novelty detection processes, our findings are generally consistent with the multiple component view advanced by Addis and Schacter (2012), which holds that the hippocampus contributes to several distinct processes that support imagining future events, including recombining event details into coherent scenarios.

Critical to the theoretical success of future studies will be mapping different subregions of the hippocampus to specific component processes using refined methods that allow for the closely related processes of retrieval, construction, and encoding to be differentiated. Employing high-resolution imaging may prove particularly useful to future progress as this method can reveal anatomy at the resolution of individual hippocampal subfields (Kerchner et al., 2010). As the hippocampus does not work in isolation, future studies should also develop approaches and theoretical models that directly evaluate how these component processes interact with the other processes embedded in the wider network supporting imagination.

Beyond the hippocampus, imagining and re-imagining events robustly recruited the distributed network associated with memory, future-thinking and related functions compared to our semantic control task (Buckner & Carroll, 2007; Schacter et al., 2007; Spreng et al., 2009). The results from the current study draw particular attention to the role of the superior frontal gyrus (BA8) and the posterior precuneus. In regard to the activation of superior frontal gyrus for imagined relative to re-imagined events, there is converging evidence that right lateralized activity in the superior and middle frontal gyrus is associated with inhibitory processes mediating controlled retrieval and encoding processes, such as suppressing the retrieval of unwanted learned associations (Anderson et al., 2004; Depue et al., 2007; Wylie et al., 2008; Rizio & Dennis, 2013). This observation raises the intriguing—though speculative—possibility that the superior frontal gyrus may contribute to processes that actively isolate episodic details from their previous associations within autobiographical memories, perhaps transitively inhibiting the former associations from memory in

order for details to be effectively recombined into a novel representation. In regard to the posterior precuneus, activity in this region increased with repeated imagining of an event rather than with event novelty; this pattern seems particularly robust because it has been observed across different paradigms that require repeated imagining of future events (van Mulukom et al., in press; Szpunar et al., in press). Exploring the precise role of regions beyond the hippocampus, including the superior frontal gyrus and the posterior precuneus, in imagining future constitutes an important task for future work.

It is only during the past few years that our understanding of the functional importance of the hippocampus has extended beyond the purview of remembering past experiences to include such functions as imagining future experiences or novel scenes (Schacter & Addis, 2009; for reviews, see Buckner, 2010; Szpunar, 2010; Schacter et al., 2012). As our investigation and understanding of imagining future events grows, the neural and cognitive processes shared by memory and imagination are beginning to come into view. But it also seems clear that processes that are preferentially recruited for imagining the future can potentially offer new theoretical insights into the functions of remembering the past, because a major adaptive function of episodic memory lies in its contribution to our ability to imagine novel events. In this way, we are not strictly bound by past experiences, but instead can flexibly use past experiences to construct event simulations and plan for the future.

Acknowledgments

We thank C. Robbins for assistance with data collection and E. Herder for helpful discussions and comments on a draft of the manuscript. This work was supported by NIH grant RO1 MH060941 to D.L.S.

REFERENCES

- Addis DR, Cheng T, Roberts RP, Schacter DL. 2011. Hippocampal contributions to episodic simulation of specific and general future events. *Hippocampus* 21:1045–1052.
- Addis DR, Schacter DL. 2012. The hippocampus and imagining the future: Where do we stand? *Front Hum Neurosci* 5:173.
- Addis DR, Schacter DL. 2008. Effects of detail and temporal distance of past and future events on the engagement of a common neural network. *Hippocampus* 18:227–237.
- Addis DR, Pan L, Vu M-A, Laiser N, Schacter DL. 2009. Constructive episodic simulation of the future and the past: Distinct subsystems of a core brain network mediate imagining and remembering. *Neuropsychologia* 47:2222–2238.
- Addis DR, Wong AT, Schacter DL. 2007. Remembering the past and imagining the future: Common and distinct neural substrates during event construction and elaboration. *Neuropsychologia* 45:1363–1377.
- Andelman F, Hoofen D, Goldberg I, Aizenstein O, Neufeld MY. 2010. Bilateral hippocampal lesion and a selective impairment of the ability for mental time travel. *Neurocase* 16:426–435.
- Anderson MC, Ochsner KN, Kuhl B, Cooper J, Robertson E, Gabriell SW, Glover GH, Gabrielli JDE. 2004. Neural systems

- underlying the suppression of unwanted memories. *Science* 303: 232–235.
- Axmacher N, Henseler MM, Jensen O, Weinreich I, Elger CE, Fell J. 2010. Cross-frequency coupling supports multi-item working memory in the human hippocampus. *Proc Natl Acad Sci USA* 107:3228–3233.
- Botzung A, Denkova E, Manning L. 2008. Experiencing past and future personal events: Functional neuroimaging evidence on the neural bases of mental time travel. *Brain and Cognition* 66:202–212.
- Buckner RL (2010). The role of the hippocampus in prediction and imagination. *Ann Rev Psychol* 61:27–48.
- Buckner RL, Carroll DC. 2007. Self-projection and the brain. *Trends Cogn Sci* 11:49–57.
- Chua E, Schacter DL, Rand-Giovannetti E, Sperling RA. 2007. Evidence for a specific role of the anterior hippocampal region in successful associative encoding. *Hippocampus* 17:1071–1080.
- Cooper JM, Vargha-Khadem F, Gadian DG, Maguire EA. 2011. The effect of hippocampal damage in children on recalling the past and imagining new experiences. *Neuropsychologia* 49:1843–1850.
- D'Argembeau A, Xue G, Lu ZL, Van der Linden M, Bechara A. 2008. Neural correlates of envisioning emotional events in the near and far future. *NeuroImage* 40:398–407.
- Depue BE, Curran T, Banich MT. 2007. Prefrontal regions orchestrate suppression of emotional memories via a two-phase process. *Science* 317:215–219.
- Duncan K, Ketz N, Inati SJ, Davachi L. 2012. Evidence for area CA1 as a match/mismatch detector: A high-resolution fMRI study of the human hippocampus. *Hippocampus* 22:389–398.
- Eichenbaum H. 2001. The hippocampus and declarative memory: Cognitive mechanisms and neural codes. *Behav Brain Res* 127: 199–207.
- Gilbert DT, Wilson T. 2007. Propection: Experiencing the future. *Science* 317:1351–1354.
- Hannula DE, Ranganath C. 2008. Medial temporal lobe activity predicts successful relational memory binding. *J Neurosci* 28:116–124.
- Hannula DE, Tranel D, Cohen NJ. 2006. The long and the short of it: Relational memory impairments in amnesia, even at short lags. *J Neurosci* 26:8352–8359.
- Hassabis D, Kumaran D, Vann SD, Maguire EA. 2007. Patients with hippocampal amnesia cannot imagine new experiences. *Proc Natl Acad Sci USA* 104:1726–1731.
- Hassabis D, Maguire EA. 2007. Deconstructing episodic memory with construction. *Trends Cogn Sci* 11:299–306.
- Hurley NC, Maguire EA, Vargha-Khadem F. 2011. Patient HC with developmental amnesia can construct future scenarios. *Neuropsychologia* 49:3620–3628.
- Jones GV. 1976. A fragmentation hypothesis of memory: cued recall of pictures and of sequential position. *J Exp Psychol Gen* 105: 277–293.
- Kirwan CB, Stark CE. 2004. Medial temporal lobe activation during encoding and retrieval of novel face-name pairs. *Hippocampus* 14: 919–930.
- Klein SB, Loftus J, Kihlstrom JF. 2012. Memory and temporal experience: The effects of episodic memory loss on an amnesic patient's ability to remember the past and imagine the future. *Social Cogn* 20:353–379.
- Kerchner GA, Hess CP, Hammond-Rosenbluth KE, Xu D, Rabinovici GD, Kelley DAC, Vigneron DB, Nelson SJ, Miller BL. 2010. Hippocampal CA1 apical neuropil atrophy in mild Alzheimer disease visualized with 7-T MRI. *Neurology* 75:1381–1387.
- Kumaran D, Maguire EA. 2007. Match-mismatch processes underlie human hippocampal responses to associative novelty. *J Neurosci* 27:8517–8524.
- Lepage M, Habib R, Tulving E. 1998. Hippocampal PET activations of memory encoding and retrieval: The HIPER model. *Hippocampus* 8:313–322.
- Maguire EA, Gadian DG, Johnsrude IS, Good CD, Ashburner J, Frackowiak RS, Frith CD. 2000. Navigation-related structural change in the hippocampi of taxi drivers. *Proc Natl Acad Sci USA* 97:4398–4403.
- Maguire EA, Hassabis D. 2011. Role of the hippocampus in imagination and future thinking. *Proc Natl Acad Sci USA* 108: E39.
- Maguire EA, Vargha-Khadem F, Hassabis D. 2010. Imagining fictitious and future experiences: Evidence from developmental amnesia. *Neuropsychologia* 48:3187–3192.
- Martin VC, Schacter DL, Corballis MC, Addis DR. 2011. A role for the hippocampus in encoding simulations of future events. *Proc Natl Acad Sci USA* 108: 13858–13863.
- Mullally SL, Hassabis D, Maguire EA. 2012. Scene construction in amnesia: An fMRI study. *J Neurosci* 32:5646–5653.
- Poppenk J, Evensmoen HR, Moscovitch M, Nadel L. 2013. Long-axis specialization of the human hippocampus. *Trends Cogn Sci* 17: 230–240.
- Race E, Keane MM, Verfaellie M. 2011. Medial temporal lobe damage causes deficits in episodic memory and episodic future thinking not attributable to deficits in narrative construction. *J Neurosci* 31: 10262–10269.
- Rizio AA, Dennis NA. 2013. The neural correlates of cognitive control: Successful remembering and intentional forgetting. *J Cogn Neurosci* 25:297–312.
- Romero K, Moscovitch M. 2012. Episodic memory and event construction in aging and amnesia. *J Lang Mem* 67:270–284.
- Schacter DL. 2012. Adaptive constructive processes and the future of memory. *Am Psychol* 67:603–613.
- Schacter DL, Addis DR. 2007. The cognitive neuroscience of constructive memory: Remembering the past and imagining the future. *Philos Trans R Soc B Biol Sci* 362:773–786.
- Schacter DL, Addis DR. 2009. On the nature of medial temporal lobe contributions to the constructive simulation of future events. *Philos Trans R Soc B Biol Sci* 364:1245–1253.
- Schacter DL, Addis DR, Buckner RL. 2007. The prospective brain: Remembering the past to imagine the future. *Nat Rev Neurosci* 8: 657–661.
- Schacter DL, Addis DR, Hassabis D, Martin VC, Spreng RN, Szpunar KK. 2012. The future of memory: Remembering, imagining, and the brain. *Neuron* 76:677–694.
- Schacter DL, Wagner AD. 1999. Medial temporal lobe activations in fMRI and PET studies of episodic encoding and retrieval. *Hippocampus* 9:7–24.
- Spaniol J, Davidson PS, Kim AS, Han H, Moscovitch M, Grady CL. 2009. Event-related fMRI studies of episodic encoding and retrieval: Meta-analyses using activation likelihood estimation. *Neuropsychologia* 47:1765–1779.
- Spreng RN, Mar RA, Kim ASN. 2009. The common neural basis of autobiographical memory, prospection, navigation, theory of mind and the default mode: A quantitative meta-analysis. *J Cogn Neurosci* 21:489–510.
- Squire LR, van der Horst AS, McDuff SGR, Frascino JC, Hopkinse RO, Mauldin KN. 2010. Role of the hippocampus in remembering the past and imagining the future. *Proc Natl Acad Sci USA* 107:19044–19048.
- Szpunar KK. 2010. Episodic future thought: An emerging concept. *Perspect Psychol Sci* 5:142–162.
- Szpunar, KK, Addis, DR, Schacter, DL (2012). Memory for emotional simulations: Remembering a rosy future. *Psychol Sci* 23:24–29.
- Szpunar KK, St. Jacques PL, Robbins CA, Wig GS, Schacter DL. in press. Repetition-related reductions in neural activity reveal component processes of mental simulation. *Soc Cogn Affect Neurosci*. PMID: 23482621.
- Tulving E. 1985. Memory and consciousness. *Can Psychol* 26:1–12.
- Van Mulukom V, Schacter DL, Corballis MC, Addis DR. Re-imagining the future: Repetition decreases hippocampal involvement in future simulation. *PLOS One* (in press).

- Viard A, Desgranges B, Eustache F, Piolino P. 2012. Factors affecting medial temporal lobe engagement for past and future episodic events: An ALE meta-analysis of neuroimaging studies. *Brain and Cognition* 80:111–125.
- Wagner AD, Schacter DL, Rotte M, Koutstaal W, Maril A, Dale AM, Buckner RL. 1998. Building memories: Remembering and forgetting of verbal experiences as predicted by brain activity. *Science* 281:1188–1191.
- Weiler JA, Suchan B, Daum I. 2010. Foreseeing the future: Occurrence probability of imagined future events modulates hippocampal activation. *Hippocampus* 20:685–690.
- Wylie GR, Foxe JJ, Taylor TL. 2008. Forgetting as an active process: An fMRI investigation of item-method-directed forgetting. *Cereb. Cortex* 18:670–682.
- Yassa MA, Stark CEL. 2008. Multiple signals of recognition memory in the medial temporal lobe. *Hippocampus* 18:945–954.