The Contextual Association Network Activates More for Remembered than for Imagined Events

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The human capacities to remember events from the past and imagine events in the future rely on highly overlapping neural substrates. Neuroimaging studies have revealed brain regions that are more active for imagined events than remembered events, but the reverse pattern has not been shown consistently. Given that remembered events tend to be associated with more contextual information (Johnson et al. 1988), one might expect a set of regions to demonstrate greater activity for remembered events. Specifically, regions sensitive to the strength of contextual associations might be hypothesized to show greater activity for remembered events. The present experiment tests this hypothesis. fMRI was used to identify brain regions within the contextual association network (Bar and Aminoff 2003); regions within this network were then examined to see whether they showed differential activity during remembering and imagining. Bilateral regions within the parahippocampal cortex and retrosplenial complex responded more strongly to remembered past events, supporting work that suggests these events have more contextual information associated with them. Follow-up voxel-wise analysis demonstrated the specificity of these results, as did reanalysis of previous experimental datasets. These results suggest that a key differentiating feature of remembering and imagining is the strength of contextual associations.

Keywords: context, episodic future thought, episodic memory, parahippocampal cortex, retrosplenial complex

Introduction

Recently, research on human memory retrieval has broadened to include not only how we remember events but also how we draw upon memory to imagine novel events not personally experienced (e.g., Addis et al. 2007; Hassabis et al. 2007; Szpunar et al. 2007). These studies were motivated by a hypothesis advanced by Tulving (1985) that a common capacity supports the human ability to both remember past events and imagine future events (termed "episodic future thought" [EFT]; Atance and O'Neill 2001). Emerging evidence supports the conclusion that episodic memory and EFT rely on highly overlapping neural substrates (see Schacter et al. 2012 for review).

A central finding in this literature is that a "core network" of regions is similarly activated by both remembering and imagining, whereas relatively few regions demonstrate activation differences between the 2 types of task. Further, the only consistent differences that have been observed are in the direction of greater activity for future events than for remembered events (Addis et al. 2007; Hassabis et al. 2007; Szpunar et al. 2007; Addis et al. 2009; Szpunar et al. 2009; Weiler et al. 2010). Reports of the opposite pattern, of greater activity for remembered events, have been rare. Although several regions (primarily in visual cortex) have been linked with greater activation for

remembered past events, these were inconsistent across the 2 studies in which they were reported and, in 1 case, were observable in multivariate but not in univariate analysis (Addis et al. 2009; Weiler et al. 2010). This elusiveness of regions demonstrating preferential activation for remembering could be considered surprising: contextual information and phenomenological experiences associated with remembered events are richer than they are for imagined episodes (Johnson et al. 1988; Szpunar and McDermott 2008a). That is, relative to imagined future events, the elements of the scene (e.g., spatiotemporal context and sequence of events) are more strongly fixed and more vividly experienced for remembered events, and yet, the more robustly observed pattern of activity is greater for imagined than for remembered events. In this study, fMRI was used to investigate the hypothesis that regions that process contextual associations activate more strongly for remembered past events than for imagined future events.

The contextual association network, first described by Bar and Aminoff (2003), includes most prominently portions of the parahippocampal cortex (PHC) and the retrosplenial complex (RSC), in addition to several other cortical regions. Regions within the network activate more strongly for items that are highly associated with specific spatiotemporal contexts than for items that are weakly associated with contexts, and more generally, for items that have strong associations than for those with weaker associations (Aminoff et al. 2007; Bar, Aminoff and Ishai 2008; Bar, Aminoff and Schacter 2008). For instance, a roulette wheel, highly associated with a casino, elicits greater activity than does a roll of duct tape, which may be associated with a number of locations but has no specific "place" to which it is tied.

Although previous studies have not revealed differences in activity within PHC and RSC (Szpunar et al. 2009; see also Szpunar and McDermott 2008b), none of these studies have localized and directly interrogated contextual association regions. Instead, they have relied upon whole-brain voxel-wise analysis strategies, which offer a broader but less focused view of activity across the brain. Defining regions of interest (ROIs) from an independent localizer task and then applying them to an episodic task may reveal differential activity in PHC or RSC for remembered and imagined events, driven by the greater contextual information available for remembered events. The present experiment tests and finds support for this hypothesis.

Materials and Methods

Participants

Twenty-two participants (16 female) were recruited from Washington University in St. Louis and the surrounding area and were right-

handed, neurologically healthy, native English speakers, with normal or corrected-to-normal vision. One participant was excluded for failing to comply with task instructions, leaving a final $N = 21$ (ages 19–30 years, mean = 24.1). Informed consent was obtained from all subjects in accordance with standard Washington University human research practices. Participants were paid $25 per hour for their participation. Participants completed 2 tasks in an fMRI scanner: a context localizer task and an episodic task. Upon completion of these tasks, participants exited the scanner and completed a post-scan questionnaire (see below).

Materials

Stimuli used in the context localizer task consisted of 160 pictures taken from a stimulus set first reported by Bar and Aminoff (2003). Half were of strongly contextualized ("STRONG") objects, identified by Bar and Aminoff as being the most typical within a specific spatial context, and half were of weakly contextualized objects ("WEAK") that were weakly associated with multiple spatial contexts. Each picture was presented as a 300 × 300 pixel image in the center of the screen (screen resolution: 1024 × 768).

Episodic task stimuli consisted of 144 words, and short phrases depicting common objects, locations, and activities expanded from a stimulus set first used by Szpunar et al. (2007). Word presentation was counterbalanced such that a given stimulus was equally likely to appear in each condition across participants. All stimuli, including the fixation crosshair shown between task trials, were centrally presented to participants in 48 point Arial type.

Context Localizer Task

In this task, participants made binary decisions about the size of objects depicted on the screen (Fig. 1, top). For each image, they decided whether or not its referent would fit inside of a shoebox. Objects were presented in alternating blocks of consisting only of either STRONG or

Figure 1. Experimental design. Participants completed a localizer task to identify the contextual association network, as well as an episodic task in which they were asked to remember or imagine specific events. (Top) In the context localizer task, participants were presented with alternating blocks of strongly or weakly contextualized items. (Bottom) In the episodic task, participants were given trial-wise instructions to remember events from their past or imagine events that might occur in their future.

WEAK objects. Ten images were presented in each block, and blocks were separated by periods of resting fixation lasting 24 s. Objects within a block were presented for 1.7 s, with a 0.3-s interstimulus interval. The sequence of blocks was counterbalanced across participants. Participants indicated their decision by making button-press responses, and the hand used to indicate each response was counterbalanced across participants.

Episodic Task

This task was based on the Galton–Crovitz cuing paradigm (Crovitz and Schiffman 1974) and adapted from methods reported by Szpunar et al. (2007). Participants were asked on a trial-wise basis to either remember a specific event that occurred in their own past ("REMEMBER") or imagine a specific event that might occur in their own personal futures ("FUTURE") (see Fig. 1, bottom). A further condition, in which participants imagined President Barack Obama participating in specific events, was also included for possible comparison with previous research (e.g., Szpunar et al. 2007; Weiler et al. 2010) but is not addressed specifically in this report. In addition to orientation cues, participants were provided with a specific event probe on each trial to help participants form a specific scenario mentally (e.g., "lottery").

Each cue-probe pair was presented for 10 s. During this time, participants were instructed to remember or imagine, as appropriate, an event related to the word or phrase being presented, for the full duration of each trial. Participants were told that each envisioned event should be unique and specific in time and place. To improve design efficiency, jittered fixation periods of 2.5–7.5 s separated each trial (Miezin et al. 2000). During this time, participants relaxed, cleared their minds, and awaited the next stimulus screen.

Post-Scan Questionnaire

After exiting the scanner, all participants completed a post-scan questionnaire, which served as both a behavioral measurement of their phenomenological experiences and a manipulation check. Participants rated each event they had imagined or recalled on its vividness, on the familiarity of the event's location, and on the subjective difficulty of generating a scenario in response to the probe. At this time, each participant also identified any event for which no scenario had been generated. Further, participants gave written descriptions of randomly chosen events from each condition (6 of each condition). Participants who reported scenarios that were nonepisodic in nature or that failed to generate scenarios for over 10% of the event probes were dropped from analysis. See Supplementary Figure 1 for summary of ratings for each event type.

fMRI Data Acquisition

All images were obtained with a Siemens MAGNETOM Tim Trio 3.0T Scanner using a Siemens 12-channel Matrix head coil. A high-resolution T1-weighted sagittal MPRAGE structural image was obtained for each participant (TE = 3.08 ms, TR(partition) = 2.4 s, TI = 1000 ms, flip angle = 8°, 176 slices with 1 × 1 × 1 mm voxels; Mugler and Brookerman 1990). A T2-weighted turbo spin echo structural image (TE = 84 ms, TR = 6.8 s, 32 slices with 2 × 1 × 4 mm voxels) in the same anatomical plane as the BOLD images was also obtained to improve alignment to an atlas. Gradient field maps were collected to estimate inhomogeneities in the magnetic field for each subject. An auto align pulse sequence protocol provided in the Siemens software was used to align the acquisition slices of the functional scans parallel to the anterior commissure–posterior commissure (AC–PC) plane. Slices collected were therefore parallel to the slices in the Talairach atlas (Talairach and Tournoux 1988). Functional imaging was performed using a BOLD contrast sensitive gradient-echo echo-planar sequence (TE = 27 ms, flip angle = 90°, in-plane resolution = 4 × 4 mm). Whole-brain EPI volumes (MR frames) of 32 contiguous, 4-mm-thick axial slices were obtained every 2.0 s for the context localizer scan runs and 2.5 s for the episodic task runs. The first 4 functional images of each scan were discarded to allow for T1 equilibration effects.

A thermoplastic mask fastened to the head coil and foam pads helped stabilize head position for all participants. Headphones dampened
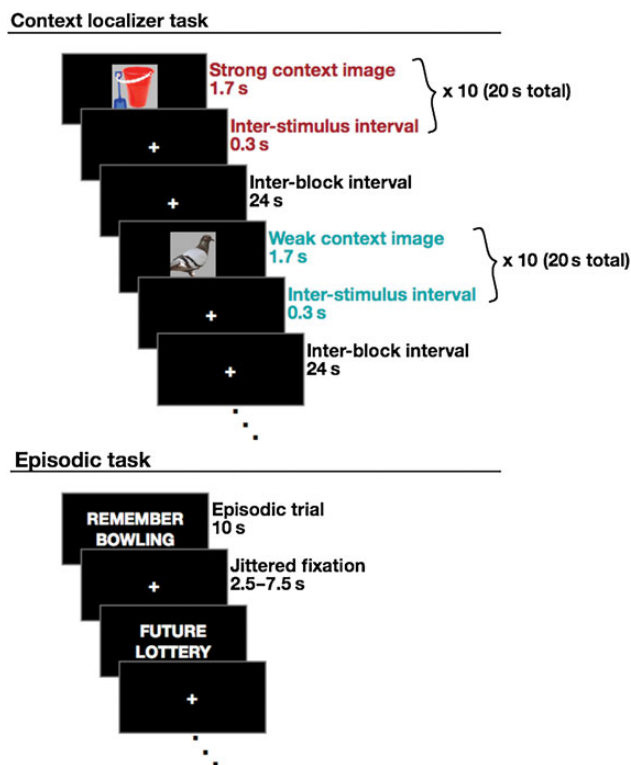
scanner noise and enabled communication with participants. An Apple iMac computer (Apple) running PsyScope software (Cohen et al. 1993) was used for display of visual stimuli. An MRI-compatible fiber optic keypress device recorded the subjects' responses during the context localizer task. An LCD projector (Sharp model PG-C20XU) projected stimuli onto an MRI-compatible screen situated at the head of the bore, which the participants viewed through a mirror attached to the coil (field of view = 21.5° of visual angle).

Data Preprocessing

Imaging data from each subject were preprocessed to remove noise and artifacts including: 1) correction for movement within and across scan runs using a rigid-body rotation and translation algorithm (Snyder 1996), 2) whole-brain normalization to a common mode of 1000 to allow for comparisons across subjects (Ojemann et al. 1997), 3) temporal re-alignment using sinc interpolation of all slices to the temporal midpoint of the first slice to account for differences in slice time acquisition, and iv) gradient field map correction to correct for spatial distortions due to local field inhomogeneities using FSL's FUGUE (http://fsl.fMRIb.ox.ac.uk). Functional data were then resampled into 3-mm isotropic voxels and transformed into stereotaxic atlas space (Talairach and Tournoux 1988). Atlas registration involved aligning each subject's T1-weighted image to a custom atlas-transformed (Lancaster et al. 1995) target T1-weighted template (711-2C) using a series of affine transforms (Michelon et al. 2003).

GLM-Based fMRI Data Analysis

Data were analyzed using a general linear model (GLM) (Miezin et al. 2000), in which the data at each time point in each voxel are treated as the sum of all effects present at that time point. For the episodic task, which was analyzed without an assumed response shape, the time course of activity for effects in each condition was modeled as a set of delta functions following the onset of each coded event (Ollinger, Corbetta, et al. 2001; Ollinger, Shulman, et al. 2001).

Context Localizer GLM Coding

Context localizer scan runs for each participant consisted of 184 MR frames (188 prior to discarding initial frames for T1 equilibration) and were concatenated into a single time series for each participant. Four runs were collected for each participant, though for 1 participant, 2 runs were dropped to within-run movement, and for a further 3 participants, only 2 runs were collected due to a programing error.

The GLMs included 2 regressors of interest, 1 for STRONG context blocks and 1 for WEAK context blocks. Regressors of noninterest included a trend term to account for linear changes in signal, and a constant term modeling the baseline signal. The estimated hemodynamic response for each task condition was modeled by a gamma function convolved with a boxcar function, with a delay of 2 s, and duration of 20 s (10 TRs). Variations in onset of the hemodynamic response were accounted for by modeling 3 additional delays of 2 s each for each condition, and using each condition's largest obtained parameter estimate.

Episodic Task GLM Coding

Episodic task runs for each participant consisted of 153 MR frames (157 prior to initial frame discarding). Six runs were collected for each participant. For a single subject, 2 runs were dropped due to within-run movement. Task trials were modeled over 10 time points. Temporal jitter introduced between trials provided a sufficient number of observations to model the BOLD response profile over time for each condition (Ollinger, Corbetta, et al. 2001; Ollinger, Shulman, et al. 2001).

Analysis and Visualization Software

Image processing was performed using Washington University's in-house fMRI processing software (FIDL; http://www.nil.wustl.edu/~fidl/) written in IDL (Research Systems, Inc.). All atlas coordinates were converted to MNI152 space using software written by Avi Snyder

and are reported in MNI152 space throughout this report. Statistical maps were projected onto a partially inflated surface representation of the human brain using Connectome Workbench software (Marcus et al. 2011).

Context Localizer Voxel-Wise t-test Analysis and ROI Definition

We conducted a voxel-wise t-test (paired sample, two-tailed) comparing activity estimates for STRONG versus WEAK context blocks for each participant. The resulting statistical maps were then averaged across individuals to create a group average contrast map (i.e., this task was used for group, and not within-subject, localization purposes). This contrast image was smoothed using a spherical smoothing kernel with 6-mm FWHM. The obtained t-test image was multiple-comparison-corrected to a whole-brain $P < 0.05$ using a $z > 3$ with at least 17 contiguous voxels (McAvoy et al. 2001). An automated algorithm (peak_4dfp) written by Avi Snyder searched for the location of peaks in the resulting image and created ROIs around them. Peaks under 10 mm apart were consolidated via coordinate averaging. ROIs were then obtained by centering a 10-mm (19 voxel) sphere, masked by the multiple comparison corrected image, about the coordinates identified by the algorithm. Regions located in white matter, CSF, or ventricles were excluded from analysis.

Episodic Task t-test Analysis and ROI Definition

We conducted voxel-wise t-tests (paired samples, two-tailed) between the REMEMBER and FUTURE event probes, aggregating activity across the 4th and 5th time points following trial onset (7.5–12.5 s following probe onset). These time points were chosen based on peak responses periods identified in prior studies (e.g., Szpunar et al. 2007; Addis et al. 2009; Szpunar et al. 2009). Smoothing, multiple comparison correction ($z > 3$, $k \geq 17$), and ROI definition for the exploratory voxel-wise analysis were conducted as described previously.

Results

Localizer-Defined Contextual Association Regions in PHC and RSC Show Greater Activity for Remembered than for Imagined Events

A localizer task was used to identify the contextual association network. Following methods described by Bar and Aminoff (2003), we compared BOLD activity in healthy subjects ($N = 21$) during trial blocks in which participants were shown strongly contextualized (STRONG) images with blocks in which participants were shown weakly contextualized (WEAK) stimuli (Fig. 1, top). A whole-brain voxel-wise t-test (paired samples, two-tailed, $\alpha = 0.05$, corrected for multiple comparisons) revealed that bilateral regions within PHC and RSC, in addition to other posterior cortical regions, showed significant STRONG > WEAK activity (Fig. 2A; see Supplementary Table 1 for full list of regions). No regions demonstrated the opposite pattern of WEAK > STRONG activity. These results are consistent with those obtained in previous studies (Bar and Aminoff 2003; Bar, Aminoff and Schacter 2008). Regions of interest were created by drawing spheres around areas of peak difference within this map (see Materials and Methods). The ROIs were then carried forward for use in the episodic task. This task provided participants with a trial-wise orientation cue to remember a past event ("REMEMBER") or imagine a future event ("FUTURE") and, in addition, provided a short word or phrase meant to help bring a specific event to mind (e.g., "lottery"; Fig. 1, bottom).

The BOLD responses associated with REMEMBER and FUTURE conditions were compared within localizer-defined ROIs using paired t-tests ($\alpha = 0.05$), and 5 regions emerged showing significant differences in activity between the 2 conditions (all
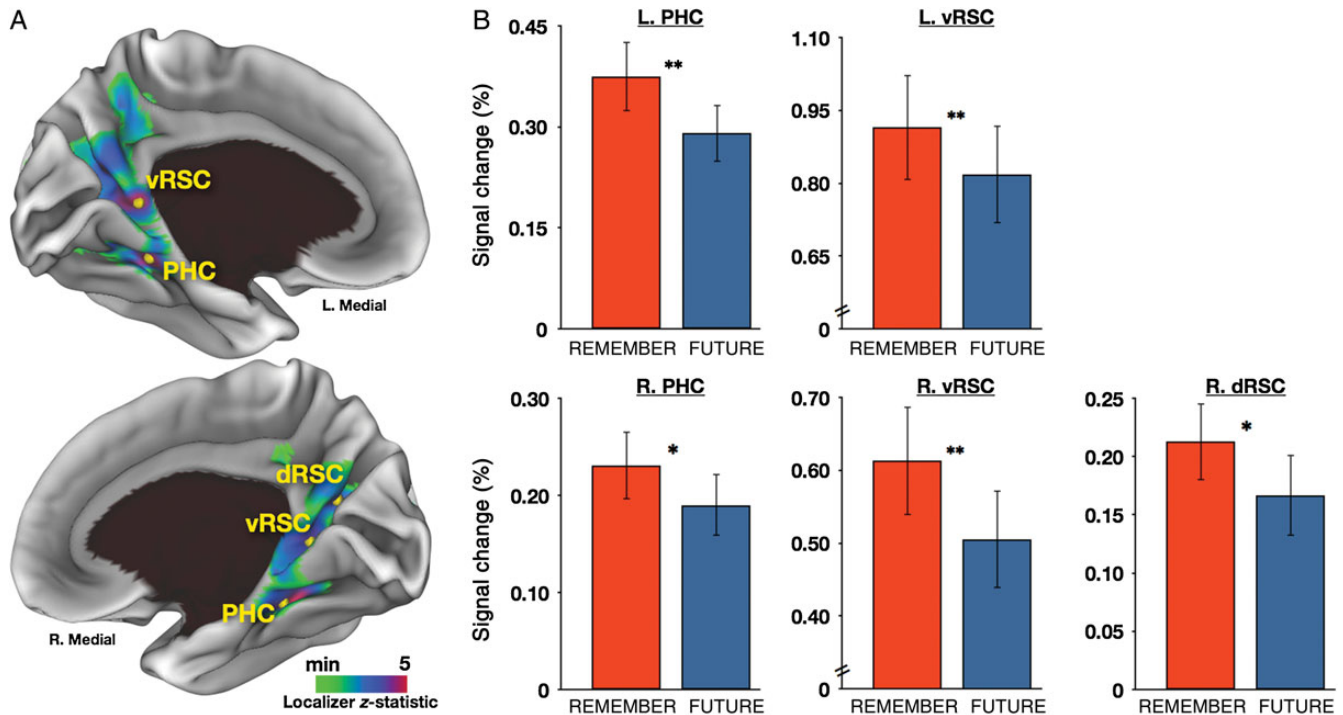
Figure 2. Regions emerging from the context localizer task also show REMEMBER > FUTURE effects. (*A*) Voxel-wise *t*-test results of the context localizer task reveal STRONG > WEAK activity bilaterally in PHC, the RSC, ventral angular gyrus, and lateral temporal cortex. An automated peak-searching algorithm identified local maxima in this contrast image, which became ROIs for use in the episodic task. Yellow nodes represent ROIs that show significant REMEMBER > FUTURE episodic effects. MNI coordinates for each region are: L. PHC, −25, −42, −10; L. vRSC, −7, −53, 8; R. PHC, 32, −36, −13; R. vRSC, 15, −52, 6; R. dRSC, 18, −61, 22. (*B*) Response magnitudes associated with the REMEMBER condition are greater than those associated with the FUTURE condition in the episodic task within ROIs shown in (*A*). Error bars denote SEM. *$P < 0.05$; **$P < 0.01$.

REMEMBER > FUTURE, Fig. 2A, yellow nodes; for response magnitudes, see Fig. 2B). The regions were located in left PHC (MNI coordinates −25, −42, −10; $t_{(20)} = 4.82$, $P < 0.001$), right PHC (32, −36, −13; $t_{(20)} = 2.5$, $P = 0.021$), left ventral RSC (−7, −53, 8; $t_{(20)} = 2.95$, $P = 0.008$), and 2 regions in right RSC, which we refer to as ventral and dorsal based upon their relative positioning (ventral RSC: 15, −52, 6; $t_{(20)} = 4.25$, $P < 0.001$; dorsal RSC: 18, −61, 22; $t_{(20)} = 2.72$, $P = 0.013$). In ROIs initially defined by a STRONG > WEAK contextual association contrast, we thus observed significant REMEMBER > FUTURE activity in an orthogonal episodic memory task.

Exploratory Analysis of Episodic Task Data Also Reveals Preferential Activity for Remembered Events in PHC and RSC

Our experiment aimed to ascertain the possible role that contextual association regions may play in differentiating between remembered and imagined events. After finding significant REMEMBER > FUTURE activity in PHC and RSC, it was important to determine the specificity of these effects in our experiment. As such, we conducted a whole-brain contrast comparing activity between these 2 conditions (Fig. 3A; see Supplementary Table 2 for full list of identified regions). Clusters showing REMEMBER > FUTURE activity were observed in left PHC (−29, −44, −8) and right ventral RSC (18, −54, 8). Each of these locations is <5 mm from ROIs defined by the context localizer task. Moreover, these 2 regions also showed significant STRONG > WEAK activity when used as ROIs to contrast activity in the context localizer task (Fig. 3B).

Applying ROIs from the Context Localizer to Previously Published Data Reveals REMEMBER > FUTURE Effects

Having shown within a single set of subjects that a context localizer could serve as a robust means of identifying regions preferentially activated for remembering, we sought to determine whether this approach would uncover similar differences in prior datasets. We selected 2 studies, previously published by this laboratory, which compared activity during remembering and during EFT.

One seemed particularly relevant in that it not only asked people to remember and imagine events but included instructions that specifically required participants to both remember and imagine these events only in familiar locations (Szpunar et al. 2009). This dataset therefore represents a fairly conservative test of the current hypothesis, as the familiarity of locations would likely reduce possible differences in contextual associative strength between the task conditions (Arnold et al. 2011). Consistent with such logic, and based on voxel-wise contrasts, this previous report had not reported differences in activity in contextual association regions. However, when we apply the ROIs derived from the context localizer within our current experiment, we found that even in this different group of subjects, the localizer-defined ROIs in bilateral PHC showed significantly greater activity for remembered events (left PHC: $t_{(26)} = 2.36$, $P = 0.026$; right PHC: $t_{(26)} = 2.09$, $P = 0.046$). We also found a nonsignificant tendency toward greater activity in the remember condition for the ROI in right dorsal RSC ($t_{(26)} = 1.67$, $P = 0.096$).

Another experiment, reported by Szpunar et al. (2007), used methods very similar to those in the present report (indeed, current methods were based upon this experiment). When
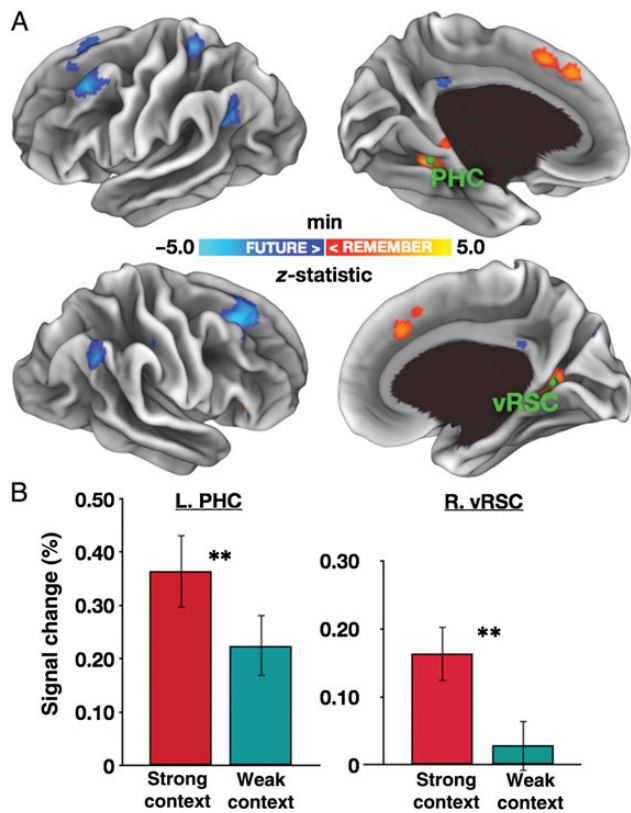
Figure 3. Voxel-wise *t*-test analysis of REMEMBER and FUTURE activity reveals a sparse set of voxels where activity differed significantly between conditions in the episodic task. (*A*) Few regions show significant REMEMBER > FUTURE activity, notably L. PHC and R. vRSC, which are identified with green nodes. (*B*) These 2 ROIs also show significant STRONG > WEAK activity in the localizer task. Error bars denote SEM. **$P < 0.01$.

applying the current ROIs to this previous dataset, we observed greater activity for remembered than for imagined events in left PHC ($t_{(20)} = 3.34$, $P = 0.003$). We also observed tendencies in this direction in bilateral RSC (left ventral RSC: $t_{(20)} = 1.77$, $P = 0.093$; right ventral RSC: $t_{(20)} = 1.75$, $P = 0.096$). Results from 2 separate datasets therefore converge upon the present findings that PHC and RSC are sensitive to the remembered versus imagined status of an envisioned event.

Discussion

In this report, regions within the contextual association network were identified as a priori ROIs, which then revealed differences in activity between remembering and imagining in a separate episodic task. PHC and RSC, previously characterized as showing similar activity when remembering and imagining, showed significantly greater activity for remembered past events than for imagined future events when thus identified. Subsequent voxel-wise analysis highlighted the specificity of these effects. These results suggest that the contextual association network plays an important role in the differential processing of remembered and imagined events. We consider possible reasons that this pattern has not been observed in previous experiments.

On the Functional Roles of PHC/RSC and Their Relevance to Episodic Thought

Reviews focusing on regions that fall within the contextual association network (Ranganath and Ritchey 2012; Aminoff et al.

2013) emphasize that regions within the network are engaged in processing links between objects and concepts that are associated within a single context (Aminoff et al. 2007). Parahippocampal cortex and RSC in particular are involved in the processing of "context frames," which represent general, schematic representations of objects, spaces, concepts, and their interrelations (Bar 2004, 2009). Participants in the present study were asked to remember specific episodes from their past or imagine specific events that might occur. It seems reasonable to hypothesize that instantiation of a context frame is an important early step when generating the specific spatial and temporal context in which a given event will occur.

Under this hypothesis, remembered events are associated with a single spatiotemporal context (episode), whereas associations for imagined future events are taken from multiple episodes, with variability in the strength of associated contexts (Fig. 4, left). The commonality of the source context for remembered events, as compared with the discrepant sources for imagined events, results in an increase in associative strength for remembered events, and this in turn is reflected in differential activation levels observed in PHC and RSC (Fig. 4, middle and right). Though we argue here that the single source of association leads to greater associative strength for remembered events, it may also be the case that another mechanism, which perhaps produces an interference-like effect, is present for imagined conditions that draw from multiple contextual sources. Future work will need to directly examine this possibility.

Our hypothesis presents a complement to the constructive episodic simulation hypothesis first forwarded by Schacter and colleagues (e.g., Schacter and Addis 2007). However, rather than focusing on the common processing that is necessary to either remember or imagine events (e.g., Addis and Schacter 2012), or specifically discussing why certain regions show a pattern of FUTURE > REMEMBER activity, we highlight the importance of an event's contextual associative strength in distinguishing remembered events from imagined events (which show a REMEMBER > FUTURE pattern). The ROIs highlighted in this report were not previously associated with a pattern of FUTURE > REMEMBER activity but, rather, are in regions that historically show approximately equal activity. Particular attention should be drawn to the distinction between retrosplenial regions, highlighted in this report, and regions in the posterior cingulate cortex, which are commonly discussed in this literature, but show very different effects. Posterior cingulate regions are more active when imagining (Fig. 3; see also, e.g., Addis et al. 2007; Addis et al. 2009), whereas retrosplenial regions (which extend into the parietal-occipital sulcus) are more active during remembering. These data suggest that these 2 adjacent parts of cortex are performing different computations, though the nature of this distinction will need to be clarified in future work.

Regarding Previous Studies and the Absence of Observing this Pattern

As noted in the Introduction, studies have generally focused on regions showing significantly greater activity for imagined future events than for remembered past events, or on regions demonstrating similar activity across these task conditions. The regions we identify in this report are among those reported in the latter category, in that they have not typically shown
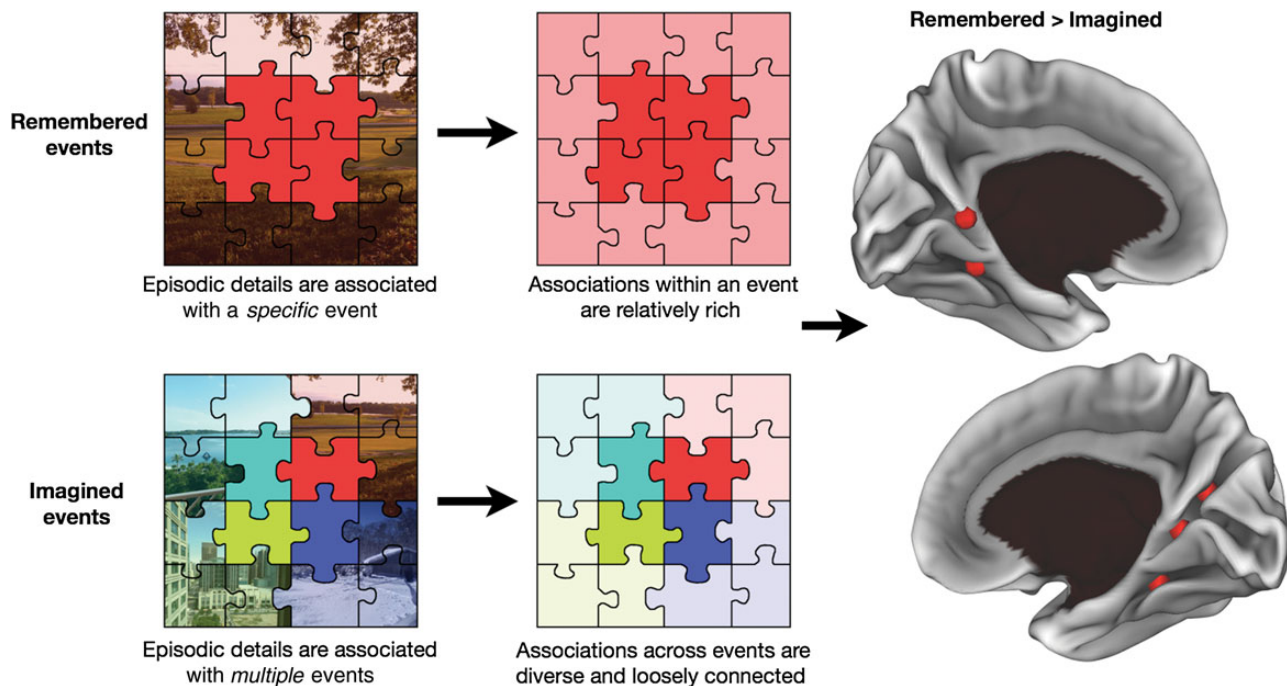
Figure 4. Proposed framework of how remembered and imagined events are differentially processed in the brain. Left: Remembered events are comprised of a collection of details that originate from the same experience (or event), whereas imagined events are generated from a combination of multiple different experiences. Middle: The common source of the remembered event details provides strong contextual associations with other components of that event, whereas the multiple sources of imagined events result in reduced overall associative strength. Right: This difference in contextual associative strength results in increased activity for remembered events in PHC and RSC.

differences between REMEMBER and FUTURE conditions. The present results are therefore a departure from previous literature (but see Addis et al. 2009; Weiler et al. 2010). How might we account for this discrepancy?

We note that constraining task conditions is a prominent concern in experiments examining episodic memory and episodic future thought. Individual trials are long (10–30 s; Addis et al. 2009; Szpunar et al. 2009), and the behaviors of interest (remembering and imagining) are covert. Participants have often recalled components of some or all events prior to being scanned (Hassabis et al. 2007; Addis et al. 2009), which can change the obtained BOLD response due to neural priming (Szpunar et al. 2014). Additionally, the long trial durations tend to reduce the number of observations in an experiment, with 20–30 total trials per condition being typical (e.g., Addis et al. 2007; Szpunar et al. 2007; Addis et al. 2009; Weiler et al. 2010).

A potential lack of constraint, combined with a small number of observations, suggests that trial-wise variability is a likely reason for previous studies failing to find differential activity in PHC and RSC (Hassabis et al. 2007; Szpunar et al. 2007; Szpunar et al. 2009). In contrast, the current design had 2 major advantages as compared with previous studies. For one, this experiment used approximately twice the number of trials typical for experiments of this sort, granting the current experiment more statistical power. This is evident in the finding of REMEMBER > FUTURE effects in our own voxel-wise *t*-test analysis, which have not been shown in mass univariate analysis in previous studies (for related discussion, see Addis et al. 2009). Furthermore, if we only examine half of our experimental trials per condition (which matches the number of stimuli presented by Szpunar et al. 2007; Szpunar et al. 2009), contextual association regions no longer emerge from a

multiple-comparison corrected voxel-wise *t*-test analysis of the REMEMBER and FUTURE conditions.

Additionally, by defining ROIs independently with the context localizer task, we were able to examine contextual association regions with higher sensitivity than were previously possible. Indeed, use of the present subjects' localizer-defined ROIs was sufficient to observe greater activity for remembered than that for imagined events in several previous experiments, reflecting that the effects observed here are not specific to this current cohort but are a core component of how remembering and imagining differ. Combining these results with the concerns of power outlined earlier, one might expect that REMEMBER > FUTURE effects were present in the Szpunar et al. (2007) and Szpunar et al. (2009) datasets but fell below threshold in voxel-wise analyses. This is indeed the case. If one lowers the statistical threshold to an uncorrected $P < 0.05$ in voxel-wise analyses of the Szpunar et al.'s datasets, PHC and RSC regions emerge showing REMEMBER > FUTURE effects similar to those observed in the present report.

In this report, we highlighted a novel role for the contextual association network in showing preferential activity for remembered events relative to imagined events. We hypothesize that issues related to trial-wise task performance variability may have masked these differences in prior work, though such an explanation requires further exploration. This new knowledge informs psychological and neuroscientific understanding of the ubiquitous, though inherently subjective, human experience of remembering.

Supplementary Material

Supplementary material can be found at: http://www.cercor.oxford journals.org/.

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